Psych 242 Notes - Lecture note Entire Semester

Physiological Psychology (University of Saskatchewan)

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What is Biopsychology? 09/08/2016

- **Biopsychology:** studying human behavior and mind from a biological perspective
- Learning Approach: history of rewards and punishments
- Personality Approach: values, interests, motivations etc.
- Psychodynamic Approach: unconscious, repressed impulses
- Social Approach: reaction to the real or imagined presence of others
- Biological Approach: functioning of hormones, organs and systems (especially the nervous system) as they relate to behavior
- - there is no single approach that is right
- - converging operations are best
- **Danielle House**
  - Miss Newfoundland → Miss Canada
  - Threw it all away when she got into a bar fight with her ex-boyfriends new girlfriend
- **Terms**:
  - **Neuroanatomy**: the study of the **structure** of the nervous system
  - **Cognitive Neuroscience**: the study of the **neural basis of cognition**
  - **Physiological Psychology:** the study of the neural mechanisms of behavior through the direct manipulation and recording of the brain in controlled experiments **usually though surgical or electrical methods (often with animals)**
  - **Neurophysiology:** the study of **the functions and activities** of the nervous system
  - **Neurochemistry**: the study of the **chemical bases of neural activity**
  - **Comparative Psychology:** the study of the evolution, genetics, and the adaptiveness of behavior by **comparing behavior across different species**
  - **Neuropsychology:** the study of the psychological **effects of brain damage** in human patients
  - **Neuropharmacology:** the study of the **effects of drugs** on neural activity

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- **Psychopharmacology:** the study of the neural mechanisms of behavior using **direct manipulation of the brain with drugs (with animals)**
- **Psychophysiology:** the study of the **relation between physiological activity and psychological processes** in human beings
- **Neuropathology:** the study of nervous system **disorders**
- **Neuroendocrinology:** the study of the interactions between the nervous system and the **endocrine system**

Jimmy G.

- 49 year-old guy believed he was 19
- Suffered from severe alcoholism which lead to damage to his hippocampus
- Couldn't form new memories
- Malnourished humans and animals can suffer similar damage without alcohol
- Alcohol can accelerate the brain damage, but is not the major cause
- Alcohol causes loss of appetite which leads to thymine deficiency
    - Approaches contributing to case study include:
        - Comparative Psychology
        - Neuropsychology
        - Neuropathology

Methods Biopsychologists Use:

- *Experiments
- ex. Give students Heroine and Cocaine throughout the semester and see who does better on the final
    - Independent and Dependent variables
    - Control groups
    - Designs
        - Between subjects ex. Half the class receives Heroine and the other half receives Cocaine every class
        - Within subjects ex. Everyone gets all conditions in stages
        - Mixed ex. Counter balance. Mix up the order of conditions.

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        - Cocaine → Placebo → Heroine
        - Placebo → Heroine → Cocaine
        - Heroine → Cocaine → Placebo
    - Experiments can reveal causation, when other methods cannot
    - Experiments cannot always be conducted due to **ethics**

- **Other Methods**
  - Quasi Experiments
    - Use subjects who are already in required conditions
      - Ex. Students who already use drugs
  - Correlational analyses
  - Case Studies
    - Ex. Finneas Gage frontal lobe damage because of a railroad spike lead to personality change
  - Technology for brain imaging and recording
- **Critical Thinking**
  - Healthy skepticism
  - Alert to weaknesses in arguments
  - Evaluation of evidence
  - Alternative explanations
  - Consider the source – validity (peer-reviewed, unbiased)
- **José Delgado** (failure of critical thinking)
  - Claimed he could control aggression by stimulating a certain part of the brain
  - Implanted an electrode in a bull's brain and by clicking a button stopped a bull from charging mid run
  - Bull could have stopped at the press of the button because it could have instead been confused, in pain, distracted, or the electrode was hitting a part of the brain responsible for direction (simulating a motor movement)
- **Lobotomy**
  - Study on one chimp showed that a lobotomy made its behavior more manageable
  - After one study on the chimp they started doing lobotomy's on "difficult people" to try and make them more manageable
  - Not enough research to support claims

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- Many surgeries ended in permanent institution

- **Rosemary Kennedy**
  - John F. Kennedy’s sister
  - Given a lobotomy, left with permanent brain damage
  - They claimed she had a mental disability and they gave her a lobotomy so she would “be more manageable”
  - She was institutionalized for the rest of her life

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- Give me a dozen healthy infants, well-formed, and my own specified world to bring them up in and I'll guarantee to take any one at random and train him to become any type of specialist I might select – doctor, lawyer, artist, merchant-chief and yes, even beggar-man and thief, regardless of his talents, penchants, tendencies, abilities, vocations, and race of his ancestors – John B. Watson
  - He believed we were born blank slates, and our experiences shaped our behaviors
- **Zeitgeist:** the ingrained general intellectual climate of our culture
- **-** it used to be whatever the Church said was truth
-
- **Where do we think?**
  - People used to believe that are thinking happened in the soul
  - People refused to believe that a human brain could be responsible for thought
  - **Monism**=the mind is the activity of the brain
  - **Cartesian Dualism**= the brain and the mind are separate (Rene Decarte)
    - Decarte: universe is made of 2 elements
      - Physical matter that behaves according to nature
      - Human mind (soul, self and spirit) which lacks physical substance, controls human behavior, and obeys no natural laws
  - The brain and the mind are really the same thing
    - It's a process of thinking and remembering and so on
  - The brain in action is thinking
- **Two misleading dichotomies in Biological Psychology**
  - **Nature versus Nature**
    - Actually a complex interaction
  - **Physiological and Psychological (brain versus mind)**
    - The mind is the activity of the brain
    - Julien Offroy: published a "scandalous" pamphlet in Europe that said thought was produced by the brain
    - **Evidence against** physiological/psychological thinking

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- The assumption that some aspects of human psychological functioning are so complex that they could not be the product of a physical brain
- Some non-human species (primate species) possess some abilities that were once assumed to be purely psychological

- **Cases**
  - **Oliver Sack's** account of the man who fell out of bed because he had **asomatognosia** (a deficiency in the awareness of parts of one's one body, and results in damage to the right parietal lobe) he didn't know where his leg was, when it was clearly still attached
  - even non-humans are capable of psychological complexity (self-awareness)
- **Ethology:** the study of animal behavior in the wild
- **Instinctive behaviors:** behaviors that occur in all like members of a species
- **Evolution**
  - The genome of modern humans is the product of evolution over many millennia
  - 1. Evolution influences the pool of behavior-influencing genes available to the members of each species
  - 2. Experience modifies the expression of an individuals genetic program
  - 3. Each individuals genes initiate a unique program of neural development
  - 4. The development of each individuals nervous system depends on the interaction of genes and experience
  - 5. Each individuals current behavioral capacities and tendencies are determined by its unique patters of neural activity, some of which are experienced as thoughts, feelings, memories, etc.
  - 6. Each individuals current behavior arise out of interactions among its ongoing patterns of neural activity and its perception of the current situation
  - 7. The success of each individuals behavior influences the likelihood that genes will be passed on to future generations
  - **evolve:** undergo gradual orderly change

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- **fitness:** is the ability of an organism to survive and contribute its genes to the next generation
- **How does evolution occur?**
    - Natural selection, survival of the fittest
    - Natural selection of individuals with traits that give them a reproductive edge over others (it isn't just about surviving, but also passing on those genes to the next generation)
    - You can pass genes without reproducing
        - You share genes with siblings, (50%) **(inclusive fitness)**
- **Evidence**
    - Fossil record
    - Homologous traits (similar traits between species)
    - Darwin's finches
    - Artificial selection (selective breeding)
        - Select certain traits they want to exaggerate
    - Direct observations of evolution
        - Moths in London
        - At first there were more white moths than black, the trees became black from pollution → More black moths bred together because there was a bigger population of them (white moths were dying off quicker because they couldn't blend in with their surroundings)

Who is more likely to pass on their genes?

- A baby that is nurtured by its mother as opposed to one that is constantly abandoned
- It isn't just physical traits that contribute, but also social traits
    - **Social dominance** is adaptive
    - Dominant and subordinate animals
        - high ranking adults have access to resource, more mates (more desirable)

Chordates: animals with dorsal nerve cords (large nerves that run along the center of the back)

Vertebrates: chordates with spinal bones (ex. bony fish)

Spandrels: the incidental non-adaptive evolutionary by-products (ex. human belly button)

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- **Exaptation's**: evolved to serve one function and were later co-opted to serve another (ex. bird wings, were originally intended for walking)
- **Homologous**: structures that are similar because they have a common evolutionary origin
- **Analogous**: structures that are similar but do not have a common evolutionary origin
- **Convergent evolution**: the evolution in unrelated species of similar solutions to the same environmental demands
- Larger animals tend to have larger brains
- **Conclusion**
  - Behavior has consequences for survival and reproduction
  - Genes influence behavior (by influencing development of the brain, body & endocrine system)
  - Behavior can evolve over time as successful genes get naturally selected
  - Behavior is the product of interactions among 3 factors
    - 1. The organisms genetic endowment which is a product of its evolution
    - 2. Its experience
    - 3. Its perception of the current situation
- **Evolutionary psychology**
  - Looking at human behavior and how we can think about it in terms of how certain kinds of behaviors are adaptive, how they can increase your reproductive success
  - Understanding human behavior by considering its adaptiveness in the face of evolutionary pressures
    - Survive when others want to kill and eat you
    - Find and hang onto the best possible mate when **conspecifics** (others in your species) also wants those mates
    - Find food for yourself and your kids when there are limited resources
    - Find shelter and warmth in a harsh climate
- **Evolutionary perspectives on sex differences**
  - Men want to spread their seed
    - Men value looks when it comes to a partner
  - Women are more focused on resources

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    - Women value money when it comes to a man (security, support for them, proving they are able)
- **Polygyny:** one male forms mating bonds with more than one female
- **Polyandry:** mating arrangement in which one female forms mating bonds with more than one male

Basic Genetics

- You inherit genes from your parents, half from mom, half from dad
- These genes (in interaction with environmental factors will determine how you develop)
- Sex-limited genes – genes are on autosomal chromosomes, but expressed only in males or only in females. They need hormonal triggers ex. breasts, and chest hair
- Sex-linked genes are on the x and y chromosomes. Because of this there is a difference in frequency. Ex. color blindness is more prominent in males because it is found on the x chromosome, and it is recessive
- **True-breeding lines:** breeding lines in which interbred members always produce offspring with the same trait generation after generation
- **Chromosomes:** the threadlike structures in the nucleus of each cell
- **Meiosis:** process of cell division that produces gametes (egg and sperm cells)
- **Zygote:** a fertilized egg cell
- What is a gene?
    - A **gene** is a section of DNA that **has a particular function**, it codes for the synthesis of a particular protein
    - For **structural genes**, the function is to direct the synthesis of particular proteins (which for structures or control physiology of cells)
    - **Enhancers** are sections of DNA that **control expression** of structural genes
    - Enhancers can be up or down regulated (more active, or less active) by proteins that bind to DNA called **transcription factors**

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- **Alleles**: variants of a gene that control the same trait
- **Homo** (alleles are the same)**/heterozygous** (alleles are different)
- **Dominant/recessive**
- **Phenotype** physical appearance of gene, the traits
- **Genotype** genetic code of gene (which alleles)
- Most traits are polygenic, (more things contribute to the trait than just the two alleles)
- Share 50% of genes in common with mom, 50% with dad and on average about 50% with siblings (sometimes more or less)
- Autosomal chromosomes: comes in matched pairs
- **Sex-linked traits:** all sex linked traits are controlled by genes on the X chromosome, because the Y chromosome is small and carries few genes

- What is **DNA**?
  - Molecule that carries genetic information, found in the nucleus of cells, and is arranged into chromosome
  - Composed into four chemical bases (nucleotides): Adenine, Thymine, Cytosine, Guanine
  - Adenine + Thymine
  - Cytosine + Guanine
  - Bases are arranged in complementary base pairs
  - **Enhancers:** stretches of DNA whose function is to determine whether particular structural genes initiate the synthesis of proteins at what rate
  - **Gene expression:** determines how a cell will develop and function
  - **Mitochondria:** energy generating structures in the cytoplasm of every cell
    - Can be used as an evolutionary clock (mutations develop in the mitochondria at a relatively consistent rate)

DNA Replication

- 1. **Helicase** (an enzyme) causes DNA strand to unwind and unzip
  - base pairs will come apart, base pairs become exposed

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    - at the location where the gene is the molecule is going to unwind and unzip, but it is confined to that location
- 2. Enzyme DNA **polymerase** links exposed nucleotide bases to their complementary bases
    - moves in opposite directions on each strand
- **Complementary base pairing**
    - The two new strands are identical to the original
- **Gene Expression**
    - Two phases
        - **Transcription** of the DNA base sequence into an RNA base sequence (mRNA) messenger RNA
            - RNA is transcribed from the exposed DNA strand and then leaves nucleus for cytoplasm
            - Instead of Thymine, Uracel joins onto Adenine, that mRNA leaves cell and then goes to cytoplasm, only the mRNA strand leaves the cell, the DNA strand stays
        - **Translation** of the RNA base sequence code into a sequence of amino acids
            - 1. The strand of mRNA attaches itself to a ribosome in a cytoplasm
            - bases in RNA molecule attract bases in the cytoplasm
            - transfer RNA is in the cytoplasm, takes the amino acids from the cytoplasm, and then it creates a chain of them based on the RNA code.
            - 2. The ribosome moves along and reads (translating) the codon (3 base pairs… ex. CGG) as it goes
            - 3. Each sequence of 3 nucleotide bases (codon) instructs the ribosome to add a particular amino acid
            - this continues until the ribosome encounters a ‘stop’ codon

Epigenetics

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- the study of heritable changes in gene expression (active versus inactive genes) that does not involve changes to the underlying DNA sequence
- affects how genes are read by cells, and thus how they produce proteins (produce them at a higher or lower rate or not at all)
- leads to change in phenotype (physical and behavioral traits) without a change in genotype
- **Analogy:** think of your life as a movie…
    - Actors = cells (always going to be there, have certain roles)
    - Script = DNA sequence (doesn't change)
    - Phrases/sentences in script = genes
    - Directing = epigenetics (causes actors to behave differently, environment and experiences can cause genes to not be expressed or to be expressed, like a director tells you to smile or not smile)
- **DNA Methylation:** the reaction that occurs when a methyl group attaches to a DNA molecule, usually at cytosine sites in mammals
- **Histone remodeling:** reaction that occurs when **histones** (proteins around which DNA is coiled) change their shape and in doing so influences the shape of the adjacent DNA
    - Can either decrease or increase expression
- **RNA editing:** acting on messenger RNA than genes
- **Ontogeny:** development of individuals over their life span
- **Phylogeny:** evolutionary development of species through the ages
    - **Sensitive period:** the period (usually early in life) during which a particular experience must occur to have a major effect on the development of a trait
    - **Gene-Environment Interactions**
        - Changes in gene expressions
        - **Ex.** males personality changes some after a baby is born
            - Father feels more protective over child, less aggressive, more caring and emotional 'soft'
            - Temporary decrease in testosterone activity due to down-regulation of genes involved
    - **Epigenetic mechanisms**

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        - **DNA methylation**
            - Methyl group (molecule that has Carbon atom surrounded by 3 hydrogen atoms) attaches to DNA molecule (usually attaches to base Cytosine)
            - Reduces expression of nearby genes
        - **Histone remodeling:** histones (proteins which DNA molecule is wrapped) different kinds of molecules can attach to the tails (golf balls with tails, DNA is wrapped around balls and molecules can attach change the shape of the histones, and can cause gene to be expressed or suppressed
    - Longer –lasting effects: genes and experiences interact to direct **ontogeny** (development in a persons lifetime)
    - Consider how your social class can affect how you develop
        - Impoverished environments vs. rich environments
        - In impoverished environments genetics are more obvious
    - **Ex.** Maze dull rats did not make significantly more errors than maze-bright rats when both groups were reared in an enriched environments. In impoverished environment maze-bright rats are still doing fine, but maze-dull rats are making lots of errors
- **Phenylketonuria PKU:** high levels of phenylpyruvic acid
    - Metabolic disorder, single recessive gene
    - Lack an enzyme important for the breakdown of amino acid, phenylalanine
    - Breakdown of phenylalanine is needed for normal brain development
    - Can be avoided with a special diet early in life
    - Symptoms include: vomiting, seizures, hyperactivity, irritability and brain damage
- "Researchers have found evidence for a significant heritability of almost every behavior they have tested" - Kalat
    - **examples:**
        - loneliness
        - status seeking

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        - neuroticism
        - TV watching
        - Speed of learning a second language
        - Intelligence
        - Athletic ability
        - Political leanings
        - Sexual orientation
        - Hitchhikers thumb
        - Ear wiggling
        - Tongue curling
    - The estimated heritability of a trait can differ across populations and times (e.g. alcohol abuse during prohibition)
        - Saskatchewan was the first place in Canada to outlaw alcohol

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Anatomy of the Nervous System 09/08/2016

- **Major Divisions of the Nervous System**
  - **Central Nervous System (CNS)*** ** the division of the nervous system located within the skull and spine
    - **Brain**
    - **Spinal Cord**
  - **Peripheral Nervous System (PNS)** the division of the nervous system located outside the skull and spine
    - **Somatic Nervous System** (nerve endings interact with outside world ((5 senses))
      - **Afferent Nerves** (nerves going towards CNS… arrive)
        - Carry signals from the skin, skeletal muscles, joints, eyes and ears ect.
      - **Efferent Nerves** (nerves going away from CNS… exit, escape)
        - Carry motor signals from the central nervous system to the skeletal muscles
    - Most nerves in PNS come from the spinal cord, but there are 12 pairs of **cranial** nerves which project from the brain
      - **Cranial nerves** include only sensory nerves
        - Olfactory nerves
        - Optic nerves
        - But most contain both sensory and motor fibers
        - Longest cranial nerves are **vagus nerves** (contain motor and sensory fibers traveling to and from the gut)
        - Autonomic motor fibers of the cranial nerves are parasympathetic
        - Assess cranial nerves as bases for diagnosing (provide location and extent of tumors and other kinds of brain pathology)
    - **Autonomic Nervous System** (behind the scenes, things we aren't aware of) regulates the body's internal environment
      - **Afferent Nerves:** carry sensory signals from the internal organs to the CNS
      - **Efferent Nerves:** carry motor signals from CNS to internal organs

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- **Parasympathetic Nervous System** (rest and digest system, conserves energy) project from the brain and **sacral** (lower back) region of the spinal cord
    - act to conserve energy
    - parasympathetic changes indicate psychological relaxation
- **Sympathetic Nervous System** (stimulates (pupils widening), fight or flight) autonomic motor nerves that project from the CNS in the **lumbar** (small of the back) and **thoracic** (chest area) regions of the spinal cord
- PNS and SNS are two-stage neural paths: project from the CNS and go only part of the way to the target organs before they synapse on other neurons (second stage neurons) that carry the signals the rest of the way
- Sympathetic nerves stimulate, organize and mobilize energy resources in threatening situations
- Sympathetic changes indicate psychological arousal

Meninges, Ventricles and Cerebrospinal fluid

Meninges: protective membranes that protect brain and spinal cord

- **Dura mater:** 'tough mother' peel a grapefruit, the thick pulp surrounding fruit
- **Arachnoid membrane:** spider-web like
- **Subarachnoid space:** contains many large blood vessels and cerebrospinal fluid
- **Pie matter:** 'pious mother' which adhere to the surface of the CNS

Cerebral Spinal Fluid (CSF)

- This fluid flows throughout all cerebral ventricles
- Fills the subarachnoid space, the central canal of the spinal cord and the cerebral ventricles
- brain and spinal cord are the most well protected organ in the body
- fluid adds a lot of cushion to parts of the brain

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- **Central Canal:** small central channel that runs the length of the spinal cord
- **Cerebral ventricles:** four large internal chambers of the brain; the two lateral ventricles, the third ventricle and the fourth ventricle
- **Cerebral Aqueduct:** connect the third and fourth ventricles

 The subarachnoid space, central canal and cerebral ventricles are interconnected by a bunch of openings forming a single reservoir

- **Choroid plexuses** (networks of capillaries, or small blood vessels that protrude into the ventricles from the pia mater) might be responsible for producing CSF
- **Dural sinuses:** large blood filled spaces where excess CSF is absorbed, dural sinuses run through the dura matter and drain into neck veins
- **Hydrocephalus** (water head): when flow of CSF is blocked by a tumor. The buildup of fluid in the ventricles causes the walls of the ventricles and the brain to expand
    - Treated by draining excess fluid from the ventricles and trying to remove the obstruction

 Blood Brain Barrier

- Prevents the passage of many toxic substances in the blood from getting into the brain
- Cells of blood vessels are tightly packed (unlike in the rest of the body where the cells are loosely packed) consisting mostly of proteins and other large molecules
- Some large molecules that are critical for brain function can pass through the barrier (e.g. glucose)
- Certain areas of the barrier allow certain large molecules to pass
- Many CNS disorders are associated with impairment of the Blood Brain Barrier

 Anatomical Directions

- Rostral or anterior(nose) **/** Caudal or posterior (tail)
- Dorsal (fish have fin on back, or top of brain) **/** Ventral (front)
- Neuraxis (CNS) straight line from the back of the neck straight through body
- Lateral (away from body) **/** Medial (towards body)
- Proximal= close

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- Distal = far
- **Planes on the Human Brain**
  - **Horizontal plane:** cutting brain in half horizontally
  - **Frontal plane:** cut brain in half vertically
  - **Sagital plane:** separate hemispheres
  - **Superior:** above
  - **Inferior:** below
  - **Cross Section:** cut horizontal on spinal cord
  - **Coronal (Frontal):** cut from front to back
- **Spinal Cord**
  - Looks like a horse tail with all the nerve endings
  - Cord is protected by a spinal column, and CSF
  - **Grey matter:** composed largely of cell bodies and unmyelinated interneurons
  - **White matter:** composed of myelinated axons
  - **Dorsal horns:** two dorsal arms of the spinal gray matter
  - **Ventral horns:** the two ventral arms
- **Stains:**
  - **Golgi stain:** used to determine overall shape by using potassium dichromate and silver nitrate = silver chromate
  - **Nissl Stain:** estimates the number of cell bodies in an area

APPS:

Brain Tutor

Brain View (test option)

Cells of the Nervous System: The Anatomy of Neurons

- **Neurons**
  - Specialized cells for the reception, conduction, and transmission of electrochemical signals
  - Come in many sizes and shapes
  - **Vertebrate motor neuron** (multipolar→ multiple processes): muscle movements
    - Motor neurons transmit commands from the CNS to muscles and glands
  - **Vertebrate sensory neuron** (unipolar → one projection)

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        - Sensory neurons are specialized to receive info from the outside world
        - Vision, hearing, touch, taste, and smell all depend on specialized receptor neurons

- **3 Main divisions of neurons (10-20% of cells in neural system)**
    - **dendrites:** receive info from other cells
    - **axon:** carries signal to other cells
    - **Cell body (soma) :** Where nucleus with DNA is located
        - Contains organelles
            - Produce energy for the cell
            - Synthesize proteins and neurotransmitters
    - **Dendrites** (tree like)
        - **Dendritic spines:** not smooth, have tiny projections on them
            - Bumps increase the surface so more info transfer can happen and receive more signals from other cells
            - Involved in learning and memory
    - **Axon**
        - Usually longer than dendrites, not tapered like dendrites
        - Each neuron only has one axon, but the axon can have branches
        - Vary widely in diameter 1-25 μm 1/1000 of a mm
        - Also vary in length (can be over a metre)
        - Myelin speeds up signal transmission in long axons
    - **Soma (neuronal cell body)**
        - Shares many of the same structures and functions as other body cells
        - **Neural membrane**
            - Composed of a phospholipid bilayer (two layers of fat molecules) containing protein channels
            - Controls which substances can enter the cell and when
            - Channel proteins: certain molecules can pass
            - Signal proteins: which transfer signal to the inside of the neuron when particular molecules bind to them on the outside of the membrane

- **Classes of Neurons**

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- **Multipolar Neuron:** more than 2 processes extending from its cell body. Most neurons are multipolar
- **Unipolar Neuron:** one process from cell body
- **Bipolar Neuron:** 2 processes from cell body
- **Interneurons:** neurons with a short axon or no axon at all. These neurons integrate the neural activity within a single brain structure but do not conduct signals from one structure to another

Neurons and Neuroanatomical Structure

- 2 kinds of gross neural structures in the nervous system
  - 1. composed of primarily cell bodies
  - 2. Composed of primarily axons
- in **CNS** clusters of cell bodies are **nuclei,** and bundles of axons are called **tracts**
- in **PNS** bundles of cell bodies are called **ganglia**, and bundles of axons are called **nerves**

Glia (or neuroglia) (80% of cells) 'forgotten cells'

- The other major type of cell in the nervous system
- Can't generate action potentials like axons can, but they have other crucial functions
- Support the activities of neurons

Types of Glia Cells

- **Mircroglia**
  - The brain's cleanup crew: when neurons and glia die, microglia remove debris by:
    - Branches of the microglia reach out and sample the immediate environment
      - If they detect molecules related to damage (e.g. from injury or stroke) they travel to the area and digest the debris
      - Also remove viruses, fungi and other microorganisms that invade the brain
- **Astrocytes** 'the stars of the glial world' star shaped, largest glia
  - Also remove debris
  - **Form connections with the blood supply***
    - Control blood flow to areas of brain (e.g. dilate blood vessels during high activity)

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        - Help transfer glucose and other nutrients from blood to brain
        - Block the transfer of other substances
        - **Help synchronize the activity of neurons**
            - Wrap around the presynaptic terminals of groups of neurons with related functions
            - When several neurons are active at once, astrocytes detect this and try to sync them
                - Ex. octopus holding students in each arm, and students start jumping
            - Then, temporarily inhibit the activity of neurons they are connected to
            - When they release inhibition the neurons are all primed to respond at the same time
        - Also restrict movement of neurotransmitters away from the synapse
        - Shield synapse from other circulating chemicals
- **Oligodendrocytes**
    - In CNS
    - Glial cells with extensions that wrap around axons of some neurons in CNS. Rich in **myelin** (fatty insulating substance) the myelin sheaths they for increase the speed and efficiency of axonal conduction
    - Provide multiple myelin segments
- **Schwann Cells**
    - In PNS
    - Aids in regeneration of damaged/severed axons
    - Constitutes of one myelin segment
- Both **Oligodendrocytes and Schwann Cells** produce myelin (fatty substance that insulates the axons)
- **Radial Glia**
    - Assist in embryonic brain development: guide neurons to their proper destinations in the nervous system (called migration)
- **Glia are not always so great**

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- **Astrocytes:** when CNS neurons damaged, they move to damaged areas and digest them. This is good….. BUT it can form scar tissue that prevents neurons from re-establishing connections AND may release chemicals in large amounts, which can kill neurons
- **Microglia:** also travel to areas of damage to digest debris. BUT can release substances that cause inflammation, causing further cell damage AND have been known to digest healthy cells in the vicinity of the damaged ones

- **Divisions of the Nervous System**
- **Telencephalon:** (cerebral hemispheres)
- **Forebrain** is mainly cortex
  - the most prominent part of the mammalian brain
  - two cerebral hemispheres, four lobes (parietal lobe, occipital lobe, frontal lobe and temporal lobe)
  - the outer cerebral cortex and various subcortical structures
    - basal ganglia
    - thalamus & hypothalamus
    - limbic system – associated with emotion, learning and memory
    - **Diencephalon** (thalamus and hypothalamus)
      - **Thalamus**: (looks like an avocado) relay station from the sensory organs to the cortex. Damage results in a coma
      - **Hypothalamus:** sends messages to pituitary gland to affect the release of hormones. Involved in the feeding, flight, fighting, reproduction (also temperature control)
    - **Basal ganglia:** group of structures includes caudate nucleus (tail that forms an almost complete circle, has connections to the Putamen), putamen and globus pallidus
      - Caudate nucleus and putamen are striped
      - Planning of motor movements (damage leads to conditions such as Parkinson's disease and Huntington's disease)
      - Involved in learning how to do something – procedural learning (ex. learning how to snowboard)

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- **Hippocampus**
  - Critical in storing memories for events
  - H.M had Interegrete Amnesia: had seizures so they removed his Hippocampus
- **Amygdala**
  - Important role in emotion, especially fear, rage, and aggression, recognizing facial expressions in others
  - very close in location to Hippocampus
  - also related in memory
  - important for learning new fears
- **Corpus Callosum**
  - 'nerve highway' allows left side of brain to share info with right side of brain and vice versa
  - right and left hemispheres linked by axon fiber bundles
- **Cerebral Cortex**
  - The cellular layers on the outer surface of the cerebrum (1.5-4 mm thick) on average there are 6 layers
  - We refer to it as grey matter because it has cell bodies and dendrites and most of the white tissue is myelinated axons
  - It is wrinkled because it gives more surface area. The bigger our bodies get the more brain power we need to get our bodies going, so this way we can fit more brain into the same amount of space
  - Larger body = a more wrinkly brain
  - Lobes
    - **Gyri:** are the bulges
    - **Sulci:** are the valley's
    - **Fissures:** if the valley's are big enough they are called fissures
    - **FIGURE 3.25**
- **Occipital Lobe:** contains **visual cortex**
  - Often called a striate cortex (striped appearance)

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        - Damage results in cortical blindness: eyes work, but no conscious experience of seeing anything. Impaired visual imagery abilities (don't dream as much, can't imagine things as well)
    - **Parietal Lobe:** contains the **postcentral gyrus** (primary somatosensory cortex)
        - Primary target for touch sensations
        - Different sections correspond to different parts of the body
        - Also responsible for perceiving location of body parts (signals sent from joints and muscles)
    - **Temporal Lobe**:
        - **Superior temporal gyrus**: auditory cortex; essential for processing spoken language (especially left hemisphere)
        - **Inferior temporal gyrus**: complex visual stimuli
        - **Fusiform gyrus:** face recognition
        - **Medial temporal lobe:** hippocampus and parahippocampal cortex-memory
    - **Frontal Lobe**
        - **Precentral gyrus** and premotor area: motor skills
        - **Prefrontal cortex**: integration center for all sensory info and other areas of the cortex
        - Also working memory, abstract thinking, decision making, planning, inhibition of impulses, appropriate behavior in appropriate context

- **Midbrain**
    - Small proportion of total brain in humans
    - Some midbrain structures;
        - **Tectum** (roof) contains superior and inferior colliculi: process sensory info (visual and auditory respectively) orientation toward/away
        - **Tegmentum:** contains
            - **Substantia nigra: ('black substance')**involved in voluntary movement

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        - **Periaqueductal gray (around the central aquedect)**: pain perception
        - **Red Nucleus:** involved in motor functions, in learning

- **Hindbrain**
    - Includes parts of the brain stem and cerebellum
    - **Medulla (Myelencephalon):** tract (bundle of axons (nerves)) is like a highway
        - Swelling of tissue just above the spinal cord
        - Many tracts (bundles of axons (nerves) carrying signals between brain and body
        - Origin of reticular formation: sleep, attention
        - Controls vital reflexes such as breathing, heart rate, vomiting, salivation, coughing and sneezing; also alertness/arousal
            - Has lots of nuclei (cluster of cell bodies) very important for life (control breathing, heart rate, blood pressure)
        - **Metencephalon (pons and cerebellum)**
            - **Pons** means bridge
                - Tracts form connections with higher brain centers
                - Many axons cross over from brain to opposite side of spinal cord in pons (contralateral control → right side of brain controls left side of body and vice versa)
                - Reticular formation passes through the pons
            - **Cerebellum** (means little brain)
                - Attached to the dorsal surface of brainstem (back of the brain stem)
                - Coordinating voluntary movements, maintaining muscle tone, regulating balance
                - Also involved in some cognitive functions (language, decision making etc.)

- **Neuroanatomical techniques**
    - **Electron microscopy:** info of neuronal structure
        - Coat thin slices of neural tissue with electron absorbing substance
        - Then pass a bean of electrons through the tissue on photographic film

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    - Produces very detailed 3D image
- **Neuroanatical Tracing Techniques**
    - **Anterograde:** used to trace paths of axons that are projecting AWAY from cell bodies located in a specific area
        - Injects area with chemicals
        - Chemicals are taken up by cell bodies and transported forward along their axons to their terminal buttons
        - After a few days the brain is removed and sliced
    - **Retrograde:** work in reverse
        - Trace the paths of axons projecting INTO a particular area
        - Chemicals are taken up by terminal buttons and then transported backward along their axons to their cell bodies
        -

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Neural Conduction and Synaptic Transmission

- **Resting state of a neuron**
  - Relative concentration of ions inside and outside the neuron: relatively more:
    - NA+ (sodium ions) outside the cell
    - K+ (potassium ions) inside the cell
    - Also more chloride ions (negatively charged) outside the cell; and large negatively charged proteins inside the cell
  - On balance, inside is negative relative to the outside
- **Resting Potential**
  - **Membrane potential:** electrical charge between inside and outside of cell
  - Measure electrical charge with a bolt meter
  - Most of what we know is from studying squid axons
  - **Resting potential:** The charge across a neurons cell membrane when the neuron is at rest
  - The cell membrane is **polarized** (different in two locations, outside vs. inside)
  - On average the charge is about -70 mV. Ranges from -40 to -80 mV
  - Extracellular fluid is on the outside
- **Forces acting upon ions**
  - Random movement and diffusion
  - Over time molecules and particles tend to distribute themselves evenly in a medium: they move down their concentration gradients
  - Move from areas of higher concentration to areas of lower concentration until they are evenly distributed
  - Potassium pulled in opposite directions by two different forces. Diffusion keeps pushing potassium to the exterior of the cell. Wants to move outside of the cell. Potassium wants to stay inside the cell because of the electrical connection
  - Chloride is the mirror image of potassium; diffusion pressure pushes it in, electrical force attracts it out
  - Sodium: both forces are working in the same direction. Sodium wants to move its concentration gradient to the inside of the cell, and is also attracted to the inside of the cell because of the electrical force.

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- **Why is there so much NA+ outside of the cell**
    - We need to have the resting potential because…
    - The channels are closed when the neuron is in resting state
    - As much as sodium wants to get in the cell, its not going to happen because the channels are closed
    - The potassium channels are open when the neuron is resting
- **There is some leakage of ions into and out of the cell**
    - The gate isn't perfect, and doesn't close completely
- **Why don't concentrations get out of balance**
    - **Sodium potassium pump**
        - There is an active transport mechanism that is pumping sodium out of the cell and potassium in
        - Actively pumps out potassium in 3, for 2 (constant)
        - Pumps are really important for maintaining balance
        - Uses 20-40% of your brain energy
    - Calcium pumps: actively pump calcium out of the cell
- **Electrostatic pressure (electrical attraction)**
    - Opposite forces attract (so positively charged ions tend to stay in more negatively charged areas and vice versa)

A neuron at rest does not tend to stay at rest

- certain spontaneous rate of firing even if nothing is stimulating the neuron

Action Potential

- Cell excited by sensory input or by other cells (or artificially)
- Cell becomes **depolarized** by this stimulation (i.e. difference in electrical charge across the membrane decreases – less negative relative to the outside)
- If it depolarizes enough, it will trigger an action potential- open the flood gates
- The threshold for an action potential is typically about-65 mV (varies across thresholds)
- **What will the effect be on the electrical charge inside the cell?**
    - It will become less negative relative to the outside
    - Eventually it will become more positive

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- Opening of sodium channels is followed soon after by the opening of the potassium channels
- At the start of the action potential, NA+ channels open
- Charge across membrane reverses
- Near the peak of the action potential K+ channels open. K+ starts to leave the cell
- At the peak of the action potential (40mV), NA+ channels close, but the K+ continues to leave the cell
- As K+ continue to leave, the inside becomes negative relative to the outside again
- There is a brief hyperpolarization (voltage difference because even more negative than normal)
- Potassium channels then close
- Proper ion concentration are quickly restored

What happens if the nervous system can't produce action potentials

- If not prepared properly, Tetrodotoxin (TTX) inside the puffer fish blocks sodium channels
- If sodium channels are blocked action potentials cant happen → can't breath… etc.

The all or none law

- Think of guns (when you pull the trigger it doesn't matter if you pull the trigger harder or softer, it will fire the same)
- A neuron fires or doesn't fire
- When a neuron fires, it fires at a particular strength and it always has to fire at that strength, there is no weaker or stronger firing
- The amplitude (strength) and velocity (speed) of an action potential are always the same, regardless of the intensity of the stimulus that initiated it
- Varies across neurons but consistent within a given neuron
- **Strength of a stimulus is communicated by:** by the rate of firing (the number of action potentials that occur in a row)
  - Number of neurons firing
- **Action potential convey info by:**
  - Pattern/rhythm of firing (ex. Morse code)

Propagation of action potential

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- The replication of the action potential down the full length of the axon
- Depends if the axon is myelinated or unmyelinated
- In **myelinated axons:** (salutatory ((to jump)) conduction) can be much faster
    - The signal jumps from one node of Ranvier to the next
    - No ion channels under the myelin, only at the nodes
    - NA+ ions travel quickly inside the axon until reaching another node
    - When reach a node, trigger another action potential at that spot (NA+ enters and so on)
    - Axon potentials can travel up to 100 meters/second
    - Unmyelinated axons travel at 5m/second at best
    - Myelin saves energy- less leakage and pumping required
    - Myelinated: pressing a tab key across a word doc
    - Unmyelinated: pressing the space bar across a word doc
- In **unmyelinated axons:** (passive conduction)
    - The signal must be replicated at each successive segment of the axon (e.x. like people doing the wave)
    - When NA+ ions enter the cell, they move by diffusion into the adjacent area and depolarize the membrane there
    - When threshold reached, action potential occurs at that segment and so on down the axon
    - Like a row of mouse traps on a wobbly shelf
- **Axon Potentials don't back propagate because of refractory periods**
- Usually input from one synapse will not be enough to cause an AP in post-synaptic cell (sub threshold)
- As the signal travels passively over the cell membrane towards the axon, it loses strength
- But numerous signals coming in at the same time can add up
- **Temporal summation:** rapid repeated stimulation by the same neuron adds up
- **Spatial summation:** synaptic input from several locations adds up

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- Inputs converge and are summed up. If the total depolarization is enough to reach threshold, an action potential occurs
- This is why synchronization of inputs is important.

Summation of Inputs

- Input summed at axon hillock
- Axon potential travels along axon
- An action potential may occur (it has have enough depolarization to reach the threshold in order to do this)
- As signals travel across membrane, they do lose some power as they go
  - Two types of summation
    - **Temporal (**over time) sending a lot of signals in a short space of time
    - **Spatial summation (** input info from various locations)

Not all inputs are excitatory → two types

- Example: flexing: excite some muscles, while inhibiting some
  - **Excitatory post synaptic potentials** (EPSPs)
    - Result in the opening of sodium channels in the postsynaptic membrane (NA+ enters)
    - The effect is some NA+ enters, a slight **depolarization** of the membrane, which makes the cell more likely to fire
  - **Inhibitory post-synaptic potentials** (IPSPs)
    - Result in opening of potassium channels (K+ leaves); or chloride channels (Cl- enters)
    - The effect is a slight **hyperpolarization** of the membrane making the cell **less likely** to fire
    - An inhibitory message **cannot** flow along an axon
- Unlike action potentials, EPSPs and IPSPs are **graded potentials** (they can be weaker or stronger depending on the strength of the stimulus, the all or none law does not apply here)

To fire or not to fire, that is the question

- Each neuron receives signals from numerous other cells
- Some input will be excitatory (EPSPs), some inhibitory (IPSPSs)

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- With all these conflicting messages, how does the neuron know what to do? → integration of inputs
- Ex. you can't make a decision, and you asks others what their opinion is. You have to weigh the answers
- Having both excitatory and inhibitory input creates great complexity and power in the nervous system

*With reflexes, the reaction time is often faster after a strong stimulus than after a weaker one. Given that all action potentials travel at the same speed along a given axon, how can you explain this?

- Temporal summation, the cells fire at a faster rate, sending many signals in a short amount of time → those signals sum up more quickly, and an action potential occurs quicker, making the muscles retracting faster
- How the strength of a stimulus can be communicated

*Neuron A synapses onto neuron B, which synapses onto neuron C. Presume that no other neurons or synapses are present. An experimenter finds that stimulating neuron A causes an action potential in neuron C after a short delay. However she also knows that the synapse of A onto B is inhibitory. Explain how stimulating A could result in excitation of C.

- if the second neuron is also inhibitory, if you inhibit the inhibitor, neuron C is now free to fire

Fun Facts

- **Action Potential**
  - Once an action potential starts, it can back-propagate into the cell body and dendrites, causing the dendrites to be more susceptible to structural changes responsible for learning
  - There can be physical structural changes in the neurons when we learn
- **Local anesthetics** block sodium channels and therefore prevent action potentials from occurring (administered at the dentist or doctors)
  - Example: Novocain and Xylocaine

Synapses

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- The word is from Greek synaptein: ‘syn’ (together) and ‘haptein’ (clasp)
- The two synaptic players
    - **Presynaptic cell**: the sender of the message
    - **Postsynaptic cell**: the receiver (another neuron, muscle cell, glandular cell)
    - Each of our 100 billion neurons can have thousands of synapses

- Two types of synapses: Electrical and Chemical

- **Electrical Synapses “gap junction”**
    - Channels are always open and in contact
    - Current flows directly between the cells. If one cell is activated, cell can flow right through it and activate another cell
    - Pro: speed – nearly instantaneous transmission
    - Functions: not well understood; one appears to synchronize activity of like cells
    - Gap is 3.5 nanometers wide
- **Chemical Synapses**
    - Bulk of synapses in humans
    - Cells send chemical messengers across gaps 20-30 nanometers wide vs. 3.5 nanometers of electrical synapses
    - Slower transmission than electrical synapses (0.3 milliseconds compared to several milliseconds)
        - One wing flap of a bee is 5 milliseconds
        - **Postsynaptic processes**
            - Neurotransmitter crosses gap and binds to receptors in postsynaptic membrane
            - Receptors contain recognition molecules that respond only to certain types of neurotransmitters
            - **The Lock and Key model**
                - One key can open several different locks
            - Binding of NTS causes ion channels to open, allowing ions (NOT NTS) to enter the postsynaptic cell

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- These are called 'ligand-gated' or 'transmitter-gated' channels

- Two major types of receptors:
- **Ionotropic** receptors
  - Receptor site is attached to the ion channel
  - Binding of NT causes channel to open, ions enter channel
  - Effects are fast (<1millisecond) but short lived (only a few milliseconds)
  - Good for conveying visual and auditory info to the brain (these reflexes are good for changes that happen very quickly
- **Metabotropic** receptors (more common)
  - Receptor site is not on the ion channel, but is nearby in the membrane
  - Contains a special protein called a G protein on the intracellular side
  - When the NT binds, causes G protein to detach from receptor
  - In some cases, it binds to ion channel inside the cell, causing it to open
    - NT binds to a receptor
    - → The receptor releases a G protein which binds to an ion channel
    - → The g protein causes the ion channel to open and ions pass through
  - G protein can also activate other chemicals inside cell called **second messengers**;
    - These diffuse through cytoplasm and have various effects such as;
      - Bind to ion channels on inside of surface of membrane, causing them to open or close (causing EPSP or IPSP)
      - Trigger synthesis of a second messenger
        - Diffuses through cytoplasm and has various effects
          - Ex. can enter nucleus and bind to DNA introducing gene expression
  - Metabotropic effects are slower to start (30 milliseconds or more after NT release), but are more diffuse and last longer. Good for enduring sensations and experiences (tasting, and emotions)

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- A special type of metabotropic receptor: **Autoreceptor**
    - Some NT the cell releases binds to these receptors
    - Allows cell to monitor its own activity
    - Affects rate of NT release and also NT synthesis

Why don't NTs keep binding continuously?

- Reuptake: Some gets taken back to presynaptic cell to be recycled and reused
- Enzymatic Degradation: Some of the NT will be degraded

Neurotransmitters

- Chemicals released by a neuron into a synapse that have an effect on other neurons
- Over 100 different chemicals

Major categories of NTs

- **Small molecule NTs**: various types
    - Synthesis and packaged in the terminal buttons
    - Released in pulses with each action potential
    - **Conventional**
        - **Amino acids**
            - Glutamate (main excitatory NT)
            - Aspartate
            - Glycine
            - GABA (main inhibitory NT)
        - **Monoamines** (from one amino acid)
            - **Catecholamine** (from Tyrosine) (shared pathway for synthesis)
                - Dopamine
                - Epinephrine
                - Norepinephrine
            - **Indolamines**
                - Serotonin ("5-HT") (synthesized from Trytophan)
        - **Acetylcholine** (muscle contraction)
    - **Unconventional**
        - **Soluble gases**
            - Nitric oxide (helps blood vessels to dilate)
            - Carbon monoxide

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        - **Endocannabinoids** (chemicals that are naturally present, similar to the chemicals in cannabis) (similar to delta-9-tetrahydrocannabinol – the active ingredient in cannabis)
            - Anadamide
    - Categorized according to similar in molecular structure and how they are synthesized
    - Neurons tend to have a primary NT that they release: dopaminergic (dopamine), cholinergic (acetylcholine), adrenergic (epinephrine) etc.
- **Large NTs – neuropeptides**
    - Short chains of amino acids
    - Synthesized in cell body transported to terminals
    - Released gradually as calcium ions in cell increase
    - **5 categories** of neuropeptides
        - pituitary peptides
        - hypothalamic peptides
        - brain-gut peptides
        - opioid peptides
        - miscellaneous peptides

the big 7 NTs

- Glutamate -major excitatory NT
- GABA (Gamma-aminobutyric acid) -major inhibitory NT
- Dopamine (DA)- pleasure and reward
- Norepinephrine (NE) – sympathetic activation
- Serotonin (5-HT) – sleep, mood
- Acetylcholine (Ach) – muscle contraction
- Endorphins – analgesia (pain relief) (endogenous morphine)

Pharmacology: the use of drugs to study NT function and behavior

- Two main types of effects
    - **Agonistic**
        - Facilitating the effects of NT
        - Mimicking NT
    - **Antagonistic**
        - Interfering with the effects of NT
        - To go against, inhibit

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- **7 steps in NT action**
  - 1. NT molecules are synthesized from precursors under the influence of enzymes
  - 2. NT molecules are stored in vesicles
  - 3. NT molecules that leak from their vesicles are destroyed by enzymes
  - 4. Action potentials cause vesicles to fuse with the presynaptic membrane release their NT molecules into the synapse
  - 5. Released NT molecules bind with auto receptors and inhibit subsequent NT release
  - 6. Released NT molecules bind to postsynaptic receptors
  - 7. Released NT molecules are deactivated by either reuptake or enzymatic degradation
- **Drugs effects**
- - the molecules could bind to the receptors and block the receptors, making it impossible for the normal molecules to bind (antagonistic)
- - bind to receptors and doesn't just bind, but also has an effect, mimicking the effects of a NT (agonistic)
- -can effect the synthesis of enzymes, increase or decrease the rate of synthesis
- **Interfering with NTS can be deadly**
  - **Ex. ACH antagonists**
    - Cobra venom: block ACH nicotinic receptors
    - Botulism (Chlostridium botulinum): inhibits ACH release
      - In both cases will result in problem contracting muscles (muscle weakness, paralysis, death)
      - Tetanus: bacteria produces a toxin that inhibits the release of NTS that inhibit ACH release (inhibit the inhibitor = excitation) causes severe and persistent muscle contraction
      - Opiates: have analgesic effects by binding to endorphin receptors in PAG (i.e. opium, morphine, heroin, oxycontin) results in pain relief, euphoric effects, cough suppressant
    - Medical applications:
      - during surgery (incisions)

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        - Botulism (Botox)

- **Thought Question**

- Suppose axon A enters a ganglion (cluster of neurons) axon B leaves on the other side. An experimenter who stimulates A shortly thereafter records an impulse travelling down B. We want to know whether B is just an extension of axon A or whether A formed an excitatory synapse on some other neuron in the ganglion, whose axon is axon B. How could an experimenter determine the answer? Try to think of more than one possible method. Presume that the anatomy within the ganglion is so complex that you cannot simply trace the course of an axon through it
    - HINTS
        - All or none law
        - Axons vs. dendrites
        - Speed of signal transfer across synapse (after it crosses a synapse, the speed slows down)
        - Staining
        - Antidromic conduction (if we artificially stimulate axon B and see that axon A is stimulating we can tell it is the same axon)
    - Measure the amplitude and speed of axon travelling. If it is different you know it's a different cell. If the speed is the same it is most likely the same cell
    - Dendrites are tapered at the end, axons are the same diameter for one axon. Measure the diameter of both axons, to see if it is the same axon
    - Inject stain into first cell and see if the second axon is stained as well
    - Cut axon, both halves will deteriorate, and die if axon B does not, then it is a different axon
    -

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- **Pharmacological Research Methods**
  - Locating neurotransmitters and receptors in the brain
  - Using chemicals to manipulate and record brain activity
  - **Immunocytochemistry**
    - A technique for visualizing proteins and peptides in cells using biomolecules that bind to them
    - Usually the biomolecule is an **antibody** designed to bind to specific proteins in brain tissue
    - The antibody is linked to a 'reporter' (e.g. a fluorescent dye)
    - Direct method: primary antibody is labeled
    - Indirect: secondary antibody is labeled, better visualization
  - **In situ hybridization**
    - Recall that nucleotide base sequences in mRNA direct the synthesis of proteins
    - We can artificially create strands of RNA with the complementary base sequences for particular proteins
    - These 'hybrid RNA' strands are then labeled with a dye or radioactive marker
    - When the brain slices are exposed to the hybrid RNA, it binds to neurons that synthesize the protein of interest
- **Using chemicals to manipulate and record brain activity**
  - Psychoactive drugs can pass through the blood brain barrier
  - **Routes of drug administration**
    - Oral (swallow)
    - Subcutaneous (inject under skin)
    - Intramuscular (directly injected into muscle)
    - Intravenous (directly into vein) gets into blood stream faster
    - Intraperitoneal (into the cavity of the body where the internal organs are) not normally done with humans, more on research animals
    - Intragastric (directly into the stomach) effective is animal won't swallow drug
  - What if the substance cannot cross the blood brain barrier?
    - With animals we can directly injection into brain (implant with a tiny glass tube (cannula), open up tube and pump drug into brain whenever needed)

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- **Stereotactic surgery**: two metal bars are used to hold head in place, measuring tools help to locate specific location on brain

- **Chemical Lesions**
  - Can selectively lesion parts of the nervous system with neurotoxins
  - Inject toxin through cannula (it doesn't spread a lot through the brain tissue)
  - Selectively destroys tissue near tip of cannula; or may destroy only certain types of neurons in the area
    - Ex. ibotenic acid (found in mushrooms)

Measuring Chemical Activity of Brain

- **2-Deoxyglucose (2-DG) Technique**
  - inject an animal with radioactive 2-DG and allow it to engage in behavior of interest
  - cells absorb 2-DG when they are active because it is similar to glucose
  - we can use the autoradiography on brain slices to see where radioactivity accumulated

Measuring brain activity and function

- Factors to consider:
  - Invasiveness
  - Spatial resolution
  - Temporal resolution
- **Imaging Methods**
  - Structural imaging
  - Functional imaging
- **Structural Imaging**
  - **X-ray Computed Tomography (CT Scanning)**
    - Computer-assisted X-ray procedure that provides a 3-D representation of the brain
    - Can't x-ray brain because it measures the bone and not the soft tissue
    - Just a snap shot of what the brain looks like at that moment
    - Not invasive

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    - **Magnetic Resonance Imaging (MRI)**
    - Using MRI in brain imaging
        - Hydrogen atoms in body spinning in random orientations
        - When a strong magnetic field is applied, the protons are pulled into alignment with it
        - A short pulse of radio waves then knocks them out of alignment
        - When the pulse ends, the protons fall back into alignment with the field
        - As they do so, they release energy, which is measured by the machine
- **Functional Imaging**
    - Functional Magnetic Resonance Imaging (fMRI)
        - (looks at the levels of oxygen in blood)
        - can get a Type 1 error, get an error just by chance
    - Positron Emission Tomography (PET)
    - Diffusion Tensor Imaging (DTI)
- **Hemodynamic methods** (study blood flow)
    - PET & fMRI (good spatial resolution, but temporal resolution is not great due to slow hemodynamic response)
        - Do not measure neuronal activity directly
        - Use blood flow or blood oxygen level as measures of neural activity
        - Measurement is at the level of brain '**voxels**' (volume pixel, an element of volume in 3D space)
        - Change in blood flow/oxygen level is taken for each voxel, as an indicator of neural activation
        - Each voxel is shaded according to the level of activation
    - **PET**
        - Shows brain activity
        - Radioactive tracer injected into bloodstream (e.g. 2-Deoxy-Glucose) overtime Astrocytes and glia cells get rid of the by-products of tracers
        - As blood travels around the body (including the brain) t carries the tracer with it

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        - As the tracer decays, gamma rays are emitted and detected by gamma ray detectors
        - Greater radioactivity in particular parts of the brain over time signals increased blood flow (increased activity) in those areas
        - A little invasive
    - **fMRI**
        - hemoglobin molecules in blood carry oxygen
        - as oxygen is used up by active neurons, the hemoglobin becomes deoxygenated
        - new blood is shunted to the area to replenish the supply of oxygen
        - fMRI measures the changes over time in concentrations of oxygenated hemoglobin (Hb) and deoxygenated hemoglobin (DHb)
        - this is called the BOLD response (blood oxygen level dependent response)
        - non invasive
        - **advantage: good spatial resolution, about 1-4 mm, depending on the size of the voxels
        - voxel size depends on the magnet, more powerful magnets allow smaller voxels
    - **Interpreting fmRI data**
        - For each voxel, determine if there is a statistically significant change in the BOLD response
        - Voxels are colored according to their level of significance and superimposed onto a structural image of the brain
        - **you are NOT looking at actual brain activity
    - **Hemodynamic response function (HRF)**
        - HRF= the change in the BOLD signal over time when activity in a brain area increases
        - **Overcompensation:** increase above baseline as oxygenated blood enters area
        - **Undershoot:** as the oxygen gets used up by cells
        - Return to baseline levels

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        - Sometimes also see an initial small dip at beginning as neurons first become more active and use up oxygen
    - **Diffusion tensor imaging (DTI)**
        - Allows us to look at connections in the brain
        - Water diffuses most rapidly in the brain through tracts (bundles of axons)
        - DTI takes advantage of this by using a method of identifying areas of rapid water diffusion
    - **Transcranial Magnetic Stimulation (TMS)**
        - NOT a measure of neural activity
        - Used to alter neural activity
        - TMS applies a brief, strong magnetic field to scalp
        - Can either activate or "deactivate" brain structures
        - observe changes in behavior

- **Recording Psychophysical Activity**
    - Direct cell recording: spatial and temporal resolution is good
    - **Electroencephalography** (EEG) (electrodes on head) – gross electrical activity, looks at waves of electrical activity and the pattern
        - Many techniques of EEG:
            - Wave form assessment (e.g. determine state of consciousness)
            - Event-related potentials (ERPs)
            - Sensory evoked potentials
        - Temporal resolution is quite good
        - Spatial resolution is not very good
        - Non invasive
    - **Magnetoencephalography (MEG)**
        - Measures changes in magnetic fields on the surface of the scalp
        - Created by underlying patterns of neural activity
        - Temporal resolution is quite good
        - Spatial resolution is not very good
        - Non invasive
- **Measurement of bodily responses**

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- Which brand of the nervous system is activated as Leonard anticipates a dinner date with Penny
    - SCR/GSR (subtle sweating)
    - Pupilometry
    - EMG (muscle contraction
    - EOG

- **Paired-image subtraction technique**
    - In PET or fMRI, comparing images of brain activity across different cognitive tasks
    - Why would we want to do such comparisons (especially when we are interested in the brain basis of just one task)
        - To isolate the activity related specifically to the task of interest
        - Discount (subtract out) activity related to incidental aspects of the task
    - E.g. if I want to see what part of brain is active when you read an emotional expression, I want to discount activity related to simply looking at faces
    - Other difficulties: **default mode** activity (daydreaming)
        - noise from random cerebral events (reduce noise by averaging)

- **Morris water maze:** tank of water with a platform. Rat inside. Rat can't see the platform because the water is milky. The rat has to swim around and find the platform. The rat eventually learns where the platform is and goes straight there. **Used to study spatial learning events**

- **Elevated plus maze: used to study anxiety and fear** because some sides of the maze are open.

- **Self stimulation paradigm**: used to study addictions, drug abuse, directly stimulating the pleasure centers

- **Conditioned defensive burying**: used to see if rat learns to fear stimulus if it is paired with noise.

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- **Lordosis:** posture that female rat takes when it wants sexual activity
- **Pelorectis:** trying to look more intimidating and puffs up

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Development of the Nervous System 09/08/2016

- **1 week after conception**
  - -zygote has three layers of cells
    - endoderm: becomes internal organs
    - mesoderm: muscles, blood vessels, bones etc.
    - **ectoderm: will become skin, hair and nervous system
- **2-3 weeks after conception**
  - dorsal surface: formation of neural plate, then groove, then tube (tube eventually forms ventricles of brain)
- **neural tube**
  - rostral (towards the front) end becomes brain and brain stem
  - the caudal end becomes the spinal cord
  - if either neural pores (cranial neuropore and caudal neuropore) fails to develop properly
    - **anencephaly:** front end (rostral) end of tube fails to develop, brain can't develop, leads to death
    - **spina bifida**: caudal ends fails to close, spinal cord ends up emerging through body leading to physical and mental disabilities
- **once a neural tube is formed:**
  - development of the nervous system involves
    - **proliferation** (neurogenesis): creation of new cells
      - new cells originate from 'progenitor' cells on inner surface of neural tube (ventricular zone)
      - at its peak 250,000 new cells are born every minute
    - **migration**: movement of the cells to their target locations
      - two types:
        - 1**. Radial:** move outward towards the surface of the cortex
        - 2. **Tangential**: cells move at a right angle
        - typically cells engage in both types of migration
      - how do they migrate?
        - **Glia-mediated migration:** they guide the neurons to their target locations
        - **Soma translocation:** chemicals help to guide migrating neurons by attracting and repelling
        - Astrocytes can also help with migration

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        - Migrate inside out, the later cells have to go further and go through network of cells that have already been formed
    - **Important for proper organization:**
        - chemicals help to guide migrating neurons by attracting and repelling them on their route
        - cell-adhesion molecules (CAMSs) help cells 'stick' to other cells during migration and to aggregate
        - gap junctions (cells that are close together, they share the cytoplasm of the cell and ions can move easily between cell) allow communication between developing cells
- **aggregation**
- **synaptogenesis**: formation of new synapses – the wiring of the brain
    - **growth cones help axons find their targets**
        - growth cones – swelling at tips of developing axons
        - have long extensions (filopodia) capable of movement
        - respond to chemical 'guide posts' in extracellular environment
    - **once an axon get into the right general area:**
        - growth cone approaches muscle fiber
        - growth cone makes contact
        - synaptic vesicles accumulate in axon terminal and synaptic receptors cluster at point of contact
    - chemicals from pre- and post synaptic cells help create synaptic structures
    - astrocytes also help out – but this is not well understood yet
    - *developing neurons are promiscuous (they'll hook up with almost anybody)
    - **Neural Darwinism**
        - Initial overproduction of cells and synapses

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        - ***Synaptic pruning:** some connections gradually strengthened, others eliminated
        - Cells that fail to make lasting successful connections die because they fail to get enough neurotrophins (e.g. Nerve Growth Factor NGF)
        - If the cell dies the synapse dies to
    - **Apoptosis:** programmed cell death
        - If cells don't make enough successful connections they are programmed to die
        - **Necrosis:** un-programmed cell death, death that happens because there is something wrong (i.e. toxins), cells disintegrate, which isn't healthy for brain
        - **Apoptosis:** before the cell dies, its gets packaged into membrane sacks so when it deteriorates the chemicals that are released attract glia cells and is orderly and not bad for the brain
    - **Myelination**
        - First seen about 24 weeks after conception in cranial and spinal nerves
        - Occurs in a caudal to rostral direction (back to front)
        - Pre-frontal lobe is at the most rostral part of the brain
        - Starts pre-natal, but takes a long time to complete even into adulthood
        - Burst of myelination around birth, continues gradually for decades
- **Do any of these processes continue though childhood into adulthood?**
    - Most post-natal growth due to:
        - Myelination
        - Synaptogenesis: happens throughout whole life
        - Branching of dendrites
        - ***Neurogenesis:** originally thought that no new neurons were formed after development but;
            - Rodents: new cells form in olfactory bulbs and hippocampus

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- Birds: new cells from in HVC (song learning area) and hippocampus
- New evidence that human adults can have neurogenesis (new cells) forming in the hippocampus
    - Evidence from carbon dating: C14 is a radioactive isotope of carbon, declining in atmosphere since early 1960's
    - C14 is in the air and it gets into the cell, and we can see how much C14 is in the cell
    - Cells have the same concentration of C14 that was present in atmosphere where the cell was born
    - Skin cells = a month
    - Muscle cells = 15 years
    - Cortex= c14 matches the concentration for the persons birth year, cortical cells are the same age as we are
    - Hippocampus: evidence of neurogenesis, we can find cells that are younger than I am, they turn over 3 times maximum in a lifespan

Speri's Experiment with Frog:

- Rotated eyeball 180 degrees
- Then they grew back to initial target locations

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Brain Damage and Neuroplasticity 09/08/2016

- **The 'plastic' brain**
  - The brain changes with experience
- **Plasticity after brain damage**
  - Possible causes of damage
    - Tumors
    - Toxic substances
    - Closed head injuries
    - Stroke
    - Infections
    - Damage due to anoxia (loss of oxygen)
    - Traumatic brain injury
- **Closed head injury**
  - A sharp blow to the head that does not puncture the brain
  - Damage is due to brain hitting skull, axons and/or blood vessels being twisted or torn
  - One of the main causes of brain injury in young adults
  - **Contusion**: damage to circulatory system causing hemorrhaging
  - **Hematoma**: pooling of blood (bruise)
  - **Concussion**: no evidence of structural damage
  - **Punch Drunk syndrome**: cognitive abilities are impaired (boxing injuries)
  - **Coup and contrecoup injuries:** getting rear ended and brain gets thrown against the inside of your skull leads to damage to frontal cortex
- **Stroke or cerebrovascular accident**
- Two types
  - **Ischemia**: most common type
    - Blood clot or obstruction of artery
    - Causes: thrombosis, embolism, arteriosclerosis (build up of fatty material in arteries, as you age they harden and it can lead to closing up the blood supply)
    - Neurons lose oxygen and glucose supply
  - **Hemorrhage:** less common

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- Ruptured artery
- Cause aneurysm (ballooning out, can burst and cause a hemorrhage)
- Neurons flooded with excess blood calcium, oxygen and other chemicals

Stroke Induced brain damage

- Neurons are deprived of blood go into panic mode: release glutamate in large amounts.
  - Glutamate is the most excitatory neurotransmitter
- Glutamate over stimulates post-synaptic neurons (NDMA receptors) causing too much CA+ and Na+ to enter cell
- This causes the cells to die, but not before they also release large amounts of glutamate
- Also get lowered activity in cells that used to receive signals from those cells, and sometimes death (**diaschisis**)
- **The main goal after someone has had a stroke is to save the penumbra!**
  - Cool the brain (slows harmful processes)
  - **Tissue plasminogen activator** (tPA), breaks up blood clots and can reduce effects of an ischemic stroke
    - Giving this to someone having a hemorrhage stroke worsens the condition
- **Since much cell is caused by overstimulation from the excess glutamate, what can be done?**
  - Reduce overstimulation of neurons
    - Block glutamate synapses
      - but we need glutamate in our brain to function
    - cannabinoids (neurotransmitters in our nervous system that are similar in structure to THC (cannabis)

Tumors (neoplasm – new growth)

- **Meningiomas**: the 'good' kind (encapsulated)
  - Lot easier to remove, very contained, grow slowly
- **Gliomas:** the 'bad' kind (infiltrating)
  - Grow quickly, Hard to remove
  - glial cells
  - most common type

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- **Metastatic tumors:** when cancer cells travel to brain via bloodstream from other sites
    - Often devastating because there can be many of them

Brain infections

- Invasion by microorganisms
    - Bacterial infections (e.g. meningitis, syphilis)
    - Viral infections (e.g. rabies, herpes encephalitis)
    - Parasitic infections (amoeba Naegleria fowerleri; pork tapeworm Taenia solium)

Neurotoxins (toxic to neurons)

- Mercury, lead, drugs, excessive NT release
    - Tardive dyskinesia's (involuntary movement of facial muscles) side effect of early anti-psychotic drugs

Neurological diseases

- Epilepsy

A person comes into emerg after having suffered a sudden onset on inability to speak and move the limbs on the right side of the body

- Stroke
- TPA Tissue Plasminogen Activator
- Stroke occurred in Brocca's area and motor areas in frontal lobe, in left side of brain

A person has suffered a cut through the dorsal root of the nerves associated with the right arm

- What would you expect to be impaired? And left intact?
    - Sensation impaired
    - Movement would be intact
- No longer using right arm
    - Tie their left arm behind back- forcing them to use their right arm

Epilepsy

- Spontaneous, recurring seizures (uncontrolled, excessive neural activity)
- **Causes:**
    - Viruses
    - Neurotoxins

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    - Head injury
    - Tumors (in temporal of frontal lobe specifically)
    - Genetic influences
    - Faulty inhibitory synapses
- TRUE/FALSE
- Seizures are defined by convulsions, tremors, rigidity, and loss of balance and consciousness:
    - False – not necessarily.
    - Seizures can also take the form of subtle changes in thought, mood, or behavior
    - To general categories of epilepsy:
        - Generalized
        - Partial

- **Parkinson's Disease**
    - Movement disorder
    - Distinguishing characteristics:
        - Tremor during inactivity
        - Muscular rigidity
        - Difficulty initiating movement
        - Slowness of movement
        - Mask-like face
    - Degeneration of dopamine producing cells in the substantia nigra
    - Treatments: dopamine agonists (L-Dopa)
        - (dopamine cannot cross blood brain barrier)
        - deep brain stimulation: stimulation of sub thalamic nucleus with stereotaxically implanted electrode
- **Huntington's Disease**
    - Progressive loss of motor abilities
    - Severe intellectual decline and dementia
    - Caused by a rare single mutated dominant gene called Huntington
    - Geneticists can tell you if you have the gene

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- **Multiple Sclerosis**
  - Attacks the myelin of the CNS
  - Axons eventually deteriorate
  - Hard scar tissue develops in the CNS (sclerosis)
    - Why?
      - An autoimmune disorder. White blood cells start to attack myelin
      - Faulty immune reaction to myelin
      - Widely varying symptoms depending on areas of degeneration
    - **Symptoms**
      - Disturbances in vision
      - Muscular weakness
      - Numbness
      - Tremor
      - Loss of coordination (ataxia)
      - Sometimes cognitive and emotional changes
      - More vulnerable if you grow up in a cold climate
- TRUE/FALSE
- **Alzheimer's** is synonymous with dementia
  - False. But Alzheimer's is the most common cause
  - Progressive loss of memory
  - Attention deficits
  - Personality changes
  - Deterioration of speech
  - Major genetic component
  - Defining characteristics
    - Neurofibrillary tangles
      - Tangles of protein in cell cytoplasm

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- Amyloid plaques
  - Clumps of scar tissue made of degenerating neurons and amyloid protein
  - Believed this may be the primary system
- Neuron loss
  - Clumps of scar tissue made of degenerating neurons and amyloid protein

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- **Neuroplasticity after Nervous System Damage**
  - 1. Degeneration: deterioration
  - 2. Regeneration: regrowth of damaged neurons
  - 3. Reorganization
- **Degeneration**
  - Cutting axons (**axotomy**) is a common way to study responses to neuronal damage
  - **Anterograde degeneration**: of distal (distal: further away from the point of origin)segment between the cut and the synapse
  - **Retrograde degeneration**: of proximal segment between the cut and the soma
  - **If** the axon makes a new synaptic contact, it may survive
- **Neural Regeneration**
  - Do not proceed very successfully in mature mammals and other higher vertebrates
  - Virtually nonexistent in the CNS
  - Possible in PNS but unlikely and problematic
  - **Best case scenario**
    - When a nerve is damaged without severing the Schwann cell sheaths (e.g. by crushing) individual axons regenerate to their correct targets
    - Schwann cell sheath still intact
    - Axon can grow through the sheath the targets
  - **Second Best case scenario**
    - When a nerve is damaged and the severed ends of the Schwann cell sheaths are slightly separated, individual axons often regenerate up incorrect sheaths and reach incorrect targets

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- Nerve is cut but still a few mm apart
- Axon grow into incorrect sheaths to wrong targets

- **Worse case scenario**
  - When a nerve is damaged and the severed ends of the Schwann cells sheaths are widely separated, there is typically no functional regeneration
  - Too much space between cut ends
  - No regeneration- formation of **traumatic neuroma**
    - This case often occurs

- **Why does regeneration only occur in the PNS?**
  - Its not necessarily the cells themselves, it's more the environment
  - Schwann cells promote regeneration
    - Release neurotropic factors which stimulate growth
    - Have Cell Adhesion Molecules (CAM) on their membranes that guide the axons
  - Oligodendroglia actively inhibit regeneration
- **What happens if an axon doesn't make it?**
  - Cell loss →Area of brain doesn't function properly
  - **Collateral sprouting** in the axons of surviving cells – take over vacant synapses
- **Neural reorganization** (closely related to collateral sprouting)
  - A segment of one brain hemisphere is damaged resulting in the loss of a particular function
  - Over time the opposite hemisphere can take over the lost function in the damaged hemisphere
  - **Learning from special cases:**
  - **How does the brain adapt to blindness?**
    - Instead of receiving input from eyes, it will receive input from other senses
    - Areas normally associated with sight are taken over by other functions (hearing, touch)
    - Areas typically devoted to other sensory functions expand
    - One effect of neural reorganization in blindness
      - Visual cortex in occipital cortex is activated by reading Braille

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        - If TMS used to inactivate cells in occipital cortex, blind people have trouble reading Braille
- **Are Phantom limbs a result of cortical reorganization?**
    - Ramachandran's hypothesis: phantom limb is caused by reorganization of somatosensory cortex
    - The amputee feels a touch on his face AND on phantom limb due to their proximity on somatosensory cortex
    - Treatment: mirror box

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Hormones and Sex 09/08/2016

- **PAGE 327,333 TEST QUESTIONS**
- **Are males and females different?**
  - Yes and No
  - Breasts, hips, body shape, hair, genitals
  - Differences are not all strictly biological, they can be **social**
    - Society expects men to be more muscular
    - Society expects females to maintain hair –shave, wax, pluck
  - "mamawawa" : men are men and women are women assumption
    - thinking in terms of opposite categories
    - female bodies do female things, vice. versa
- **Hormones influence on sex**
  - 1. Influencing the development from conception to sexual maturity of the anatomical, physiological and behavioral characteristics that distinguish one as male or female
  - 2. By activating the reproduction-related behavior of sexually mature adults
- **What determines sex?**
  - Aristotle believed it was the temperature of sperm → ridiculous
  - **Chromosomes:**
    - XX will usually develop a female anatomy
    - XY will usually develop a male anatomy
  - **Steroid Hormones**
    - Androgens more abundant in males (testosterone)
    - Estrogens more abundant in females (estrogens ie. estradiol)
    - Travel through bloodstream including across blood brain barrier
    - Can cross cell membranes (small, fat-soluble)
    - Bind to receptors in cytoplasm or nucleus and affect gene expression
- **Major Endocrine Glands** (only organs whose primary function appears to be the release of hormones are referred to as endocrine glands)
  - Pineal gland
  - Parathyroid gland

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- Kidney
- Hypothalamus*
- Pituitary gland*
- Thyroid gland
- Thymus
- Adrenal gland *
- Pancreas
- Testis*
- Ovary*

Glands

- 1. **Exocrine glands** (ex. sweat glands) release their chemicals into ducts, which carry them to their targets, mostly on the surface of the body
- 2. **Endocrine glands** (ductless glands) release their chemicals (**hormones)** directly into the circulatory system until it reaches it target (other endocrine glands or sites in the NS)

Gonads

- Up to 6 weeks, undifferentiated primordial gonads
- Male testes, and female ovaries
- Copulation: sexual intercourse
- All chromosomes look like X's once duplicated

Classes of Hormones

- **Amino acid derivative hormones**
    - Synthesized in a few simple steps from an amino acid molecule
        - Ex. epinephrine, released from the adrenal medulla and synthesized from tyrosine
- **Peptide hormones and protein hormones**
    - Chains of amino acids (peptides are short chains, proteins are long chains)
- ***Steroid hormones**
    - Synthesized from cholesterol, a fat molecule
    - Sex hormones are steroid hormones
    - Can directly influence gene expression (by binding to receptors in cytoplasm or nucleus)

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        - Have the most diverse and long lasting effects on cellular function
        - Released from gonads
        - Ovaries release more estrogens
        - Testes release more androgens
        - Ovaries and testes release **progestins** (steroid hormone) (ex. progesterone: prepares uterus and breasts for pregnancy)
        - **Adrenal cortex:** releases sex steroids released by gonads (the adrenal cortex is thought of as a sex gland)
    - ***Hormone release can be regulated by experience
        - species that only breed in spring, release of sex hormones triggered by increasing daily duration of daylight
    - hormones are released in pulses, several times a day in large surges

- **Genetic Males XY**
    - After 6 weeks**: SRY gene** (sex determining region of Y chromosome) is expressed and gonads develop into testes
    - 8 weeks: Testes produce testosterone (T), causing **Wolffian ducts** to develop into male organs
    - 12 weeks: testes also produce **Muellerian** inhibiting hormone (MIH), and Muellerian ducts degenerate
- **Genetic Females XX**
    - No SRY gene, so gonads develop into ovaries (default state)
    - No testosterone, so Wolffian ducts degenerate
    - No MIH, so Muellerian ducts develop into internal female organs
        - Note biopotentiality, to have both genitals
- **SRY genes**
    - Remove SRY gene in males, females structures develop
    - Insert it into females: male structures develop
- **Organizing/Developmental Effects of Hormones**
    - Long-lasting structural effects
    - Occur mostly at sensitive stages of development
        - **Prenatally, perinatally (around the time of birth), puberty**
    - **Estrogens** cause feminization of body (ex. estradiol)

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        - **Estradiol:** reduces brain damage associated with neurodegenerative disroders (women are less prone to these disorders)
            - Reduces inflammation
            - Encourages axonal regeneration
            - Promotes synaptogenesis
            - Increases adult neurogenesis
    - **Androgens** cause masculinization (and auxillary hair growth (armpit hair) in both sexes) (ex. testosterone)

Can hormones affect brain development?

- What does this mean in terms of sexual dimorphism in brains and behavior?
    - Male brains are larger because the larger the person is the larger the brain is

One well-known sex difference in brain function

- Gonadotropin release by the pituitary in females is cyclical, in males it's steady
    - Switched gonadotropin in male and female rats and it was still cyclical in females and steady in males
- Determined by the presence or absence of androgens during prenatal development

A sex difference in brain anatomy

- Sexually dimorphic nucleus of the preoptic area (SDN-POA) is more developed in males than females
- SDN-POA contributes to male sexual behavior
- Castration early in life leads to smaller SDN-POA in males; injecting testosterone in females makes it larger
- Mens brains are 15% larger
- Some sex differences in brains aren't manifested till puberty
- Sex chromosomes influence brain development

Aromatization Hypothesis

- All gonadal and adrenal sex hormones are steroid hormones
- All steroid hormones are derived from cholesterol, and have similar structures and are readily converted from one to another
- **Aromatization:** aromatase (found in hypothalamus) converts testosterone to estradiol

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- Perinatal testosterone does not directly masculinize the brain
- Brain is masculinized by estradiol that has been aromatized from perinatal testosterone
    - **Evidence:** 1. Findings of masculinizing effects on the brain of early estradiol injections
    - **2.** Findings showing masculinization of the brain does not occur in response to testosterone administered with agents that block aromatization or in response to androgens that cannot be aromatized (i.e. dihydrotestosterone)
    - **alpha fetoprotein:** keeps genetic females brains from being masculinized
        - Deactivates circulating estradiol by binding to it in the blood
        - Testosterone is immune to alpha fetoprotein

Do steroid hormones affect human hypothalamic development?

- In human anterieror hypothalamus**:**
    - Areas analogous to SDN-POA in rat brain
        - Interstitial nuclei of the anterior hypothalamus (INAH)
        - Especially an area called INAH-3 in medial preoptic area
        - About twice as large in human males than in females
- Steroids do not enhance sexual function
    - Cause reduction in testicular activity and sterility
    - Breast growth in men
    - Cause cessation of menstruation (amenorrhea), sterility, excessive growth of body hair (hirsutism), growth of clitoris, masculine body, baldness, smaller breasts, deeper voice
    - Effects don’t always happen right away

Masculinization and Feminization in rats- anatomy and behavior

- **Females**: testosterone injections during development
    - Enlarged clitoris
    - Mounts other females and makes thrusting movements
    - Does not engage in lordosis (a typical female behavior when aroused)
    - Female with lack of estradiol during development:
        - Physically female because of lack of androgens

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        - But fail to develop normal female sexual behaviors
- **Males:** estrogen injections during development have little effect on external anatomy
    - **Not enough androgens** during development leads to feminization of anatomy and behavior
        - Caused by:
            - Castrated
            - Lack working androgen receptors
            - Exposed to substances that interfere with androgen response
- **Sexual dimorphisms:** differences in sexual behavior

Hyenas

- Female hyenas are naturally exposed to high levels of androgens during prenatal development
    - Masculinized anatomy, also highly aggressive
    - Female hyenas have a clitoris that almost looks like a penis

Sex differences in non-sexual behaviors

- Male monkeys played with balls and trucks more than females did
- Females played with dolls and plush toys more than males did

Does this mean there is no socialization effects?

- Of course not
- **Multiplier effects:** parents strengthen small preferences
- **Culture:** expectations/attitudes about boys vs. girls
    - **Where do the expectations/attitudes come from?**
        - Brain differences in interaction with socialization

Pituitary Gland (master gland)

- Hypothalamus controls the pituitary gland
- Produces hormones that cause the release of steroid hormones (androgens and estrogens)
    - Posterior pituitary hormones: **vasopressin, oxytoxin** (peptide hormones, both influence stress coping and social responses)
        - Vasopressin: facilitates the reabsorption of water by the kidneys
        - Oxytoxin: stimulates contractions of the uterus during labor and the ejection of milk during suckling

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- Neurons originate in hypothalamus and when they get excited they have an effect on the posterior pituitary
- Blood supply from hypothalamus goes to anterior pituitary **hypothalamopituitary portal:** large capillary that brings blood down from hypothalamus
- Anterior pituitary gland releases:
    - **Gonadotrophins:** travel through bloodstream which effect the release of hormones in glands other parts of the endocrine system

- - activity in prefrontal cortex is suppressed during orgasm
- **Cortex:** mediates the most complex aspects of sexual experience
- **Ventral Striatum:** associated with the anticipation and experience of sexual activity and other pleasurable activities
- **Hypothalamus:** the ventromedial nucleus plays a role in female sexual behavior; the medial preoptic area plays a role in male sexual behavior
- **Amygdala:** plays a role in the identification of potential mating partners
- THOUGHT QUESTION
    - Imagine that a persons sex chromosomes are XY, but they have no functioning androgen receptors
        - How would their internal sex organs develop?
            - Testes will still develop and produce testosterone
            - Mullerian inhibiting hormone is still present
            - Organs don't properly develop, won't function correctly
        - How would their external sex organs develop?
            - Develop as female sex organs
        - How would they develop at puberty
            - No menstruation, sterile
            - Develop as female
        - What would their gender identity be?
            - Typically female
- **Androgen Insensitivity Syndrome** (AIS)
    - 1-60,000 XY births (1 in 2000 in North America)
    - 1 in 300 births is some ambiguity
    - Defective gene – lack androgen receptors

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- Prenatal development proceeds as if androgen levels were low
- Genetic males (XY), but feminized
    - Smaller than average penis, or female genitals
    - Breast development, broadening of hips during puberty
    - Lack of (or little) ancillary hair
    - Internal testes
    - Sometimes a shallow vagina and no female internal sex organs
    - Female gender identity and sexual behavior
        - i.e. Eden Atwood

 THOUGHT QUESTION

- What would be the effects on development of a person with genotype XX who was exposed to excessive androgens during prenatal development?
    - External organs
        - Large clitoris, fusing of labia a bit, small vaginal opening. Bit of a masculinization of organs, but nothing major
    - Internal organs
        - Will develop normally because there are no testes producing Mullarian inhibiting hormones
    - Puberty
        - Unpredictable
        - Sometimes masculinization, sometimes more feminine, sometimes its something in between
    - Gender identity
        - Unpredictable

 Congenital adrenal hyperplasia (CAH)

- 1 in 10,000 births
- excess release of androgens by adrenal gland – causes androgenital syndrome
- genetic females (XX) masculinized genitalia;
    - enlarged clitoris, labia resemble a scrotum
    - sometimes no vaginal opening, or small
    - internal sex organs usually develop normally (androgens released later in prenatal development)

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    - behavior may also be affected (tomboyish, greater interest in more typically male activates)
    - higher incidence in homosexuality, bisexuality
- at puberty, excess androgen release can cause development of secondary sex characteristics
- however sometimes estrogens can predominate at puberty

 5 alpha reductase deficiency (5-ARD) (common in Dominican Republic)

- genetic male (XY) cannot produce 5-ARD, an enzyme needed for proper development of male genitalia
- thus, ambiguous or female genitalia
- usually raised as females
- internal male sex organs are not affected
- at puberty, increase in Testosterone causes development of male sex characteristics (testes appear, normal male genitals develop)
- in 60% of cases, normal male genitals develop at that time
- typically male gender identity

 Biology and Gender

- Hormones have organizing effects on gender identity
- Beginning in 1950's babies who were born with ambiguous or female appearing genitals were raised as females
- CASE STUDY: David Reimer, victim of ablation penis
    - Twin brothers
    - Went in to get circumcised, things went wrong when using electricity and burnt off his entire penis
    - Dr. Money convinced the parents that they should raise him as a girl, construct a vagina for him and never tell the child
    - Dr. Money had an anterior motive, believed gender was largely due to socialization and they would turn out fine, had perfect subjects (twins)
    - Gave David estrogen, tried to feminize him
    - But David always felt more like a male
    - Got married, testosterone replacement therapy, adopted kids
    - David committed suicide in the end

 Activating Effects of Sex Hormones

- Enhance sensitivity of nerves in sex organs

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- Increase activity in parts of hypothalamus related to sexual behavior
- Trigger release of **dopamine** by the preoptic area (POA) of the hypothalamus = sexual arousal

- **Testosterone and sex drive** (definitely related)
  - Orchidectomized (castrated)males lose/reduce their sex drive
  - Testosterone replacement therapy restores it
  - Is variability in testosterone across individuals related to differences in sex drive?
    - According to textbook no.
    - There is contradictory evidence.
    - They don't know
- **Gonadal hormones and females**
  - **Estrous:** 12-18 hour period where female is fertile and likely to assume lordosis posture
  - Ovariectomy eliminates estrous cycle and sexual behavior in rats
  - Injecting estrogens restores them
  - In humans: ovariectomy has little effect on sexual motivation
  - With regard to fluctuations in estrogens throughout the 28 day cycle →Women are complex
  - Androgens may be more important
- **Homosexuals**
  - Don't have lower levels of sex hormones, have same levels as heterosexuals
  - Sexual choice is not a preference, its genetic
  - No reliable difference in homo and heterosexual brains
  - **Transexualism:** he or she is trapped in a body of the opposite sex

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Drug Addiction and the brains reward circuits

09/08/2016

- **Psychoactive drugs**
  - Can cross blood brain barrier
  - Influence functioning of brain and thus affect our feelings, thoughts, perceptions, behavior and experience
- **Drug Admin**
  - Taken by: orally, injection, inhalation or absorption
  - **Oral:** preferred
    - Alcohol readily passes through stomach wall, and bypasses the need to be absorbed in intestines
    - Metabolites: breakdown products of the body's chemical reactions
    - Two advantages: ease, relative safety
    - Disadvantage: unpredictability (absorption can be affected by amount/type of food in stomach)
  - **Injection:** effects are strong, fast, predictable
    - Made: Subcutaneously, (fatty tissue under skin)
      - Intramuscularly (into large muscles)
      - Intravenously (directly into veins)
      - Many drug users prefer IV because it goes from the blood stream straight to the brain → scar tissue, infections, collapsed veins at injection sites
  - **Inhalation:** mainly anesthetics (i.e. tobacco, marijuana)
    - Disadvantages: difficult to regulate the dose
    - Many substances damage lungs if inhaled consistently
  - **Absorption through Mucous Membranes** (nose, mouth, rectum)
    - (i.e. cocaine)
  - **What happens to your sensitivity to a drug if take a drug repeatedly**
    - Build up a **tolerance**
    - Decreased sensitivity to a drug over time
    - Shift in the dose-response curve to the right
    - In some cases, experienced users of a drug can tolerate dosages that would kill a first time user
  - **Aspects of Tolerance**
    - Tolerance often develops to some effects but not to others

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        - E.g. alcohol: tolerance to slurring and staggering, but not reaction time and judgment
        - E.g. anxiolytics: tolerance to sleepiness but not anxiety-reducing effects
    - **Cross tolerance**: exposure to one drug can produce tolerance to similar drugs
    - **Drug sensitization**: increasing sensitivity to a drug
    - No single mechanisms: Many kinds of adaptive changes occur to reduce drug effects

- **Drug Metabolism**
    - Eliminates drugs ability to pass through lipid membranes of cells = can't cross blood brain barrier
    - Small amounts of psychoactive drugs are passed from the body in urine, sweat, feces, breath and mother's milk
- **Drug Tolerance Mechanisms**
    - Some drugs bind to receptors; by influencing the synthesis, transport, release, or deactivation of particular neurotransmitters; or by influencing the chain of chemical reactions elicited in postsynaptic neurons by the activation of their receptors
    - Alcohol and many general anesthetics act diffusely on neural membranes throughout the CNS
        - **Metabolic**
            - Less drug is getting to the site of action (e.g. because enzymes (from liver) break it down become more efficient)
        - **Functional (for psychoactive drugs, more common)**
            - Decreased effect at the site of action: fewer receptors, decreased efficiency of binding at receptors, receptors are less responsive
        - Tolerance sometimes fails: people sometimes die after taking a dosage that is the same or smaller than what they have become accustomed to
            - Often has to do with a change in environment
            - Change in procedure
            - Taking the drug with different people
            - Different emotional state

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- **Conditioned Tolerance**
  - Maximal tolerance that occurs when a drug is consistently taken **under the same conditions**
  - ***i.e. tolerance is largely **situation specific**
    - i.e. drinking at a dinner party vs. a drink at a wine and cheese event in the middle of the day
- **Conditioned Tolerance: Mechanism**
  - taking a drug causes your body to react with opposing, protective responses to regain homeostasis
  - eventually the drug-taking context becomes associated with the drug in your brain, and your body gets very good at reacting with opposing responses even before you take the drug
    - go to a bar, brain knows what's going to happen
    - brain starts preparing for what is about to happen
  - thus if the drug is taken in a different context the opposing, protective responses are not fast or strong enough → bad news
  - each instance of drug-taking is like a classical conditioning trial
    - i.e. Pavlovian conditioning with dog and bell
    - repeating pairing of drug with context
    - conditioned response: body reacts in preparation for drug
- **Contingent Drug Tolerance:** tolerance develops only to drugs effects only after they are actually experienced
- **Conditioned Compensatory responses:** conditional stimuli that repeatedly predict the effects of a drug come to elicit greater and greater conditioned compensatory responses→ responses increasingly counteract the unconditional effects of the drug and produce situationally specific tolerance

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        - **Exteroceptive stimuli:** external, public stimuli i.e. drug admin environment
        - **Interoceptive stimuli:** internal, private stimuli

- **Conditioned tolerance in rats**
    - Experiment 1: Morphine tolerance
        - Three groups of rats:
        - Group A injected with saline for 30 days
        - Groups B and C injected with increasing doses of heroin over 30 days
        - All rats then given a lethal does of heroin after the 30 days
            - Groups A and C in same environment as before
            - Group B in a new environment
        - Group A died (first exposure to heroin)
        - Group C were mostly fine (heroin in usual environment)
        - Group B in between (in new environment)
- **Can conditioned tolerance explain drug cravings?**
    - Many people relapse after detox
    - Go to old environment where they used to take drug
    - Brain starts preparing for taking drug
    - Body starts to crave it
- **What can we do about it?**
    - Find new group of people
    - Don’t go to those old environments
    - Remodel home, new furniture
- **Why do people take drugs?**
    - social peer pressure
    - to cope
    - live on the edge
    - **pleasurable effects** (euphoria)
    - **instrumental use** (using it as a tool)
        - prescribed by doctor
        - use as a tool to be more outgoing, relax, reduce stress
    - **dependence**
- **Why do people become dependent on drugs?**
    - **Drug dependence**

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- **Physical dependence:** attempt to avoid physical withdrawal symptoms
    - Problems with this theory:
        - Some drugs don't have severe withdrawal symptoms
        - Some individuals become addicted to drugs without experiencing withdrawal symptoms
        - Detoxified addicts often relapse
        - Drug taking patterns are often on and off
            - (i.e. weekend binges)
- **Positive incentive theory**
    - User strongly craves the hedonic effects of the drug
    - Anticipation of the drug effects is an even more powerful motivator
    - Could it be our brain's fault? YES
        - Olds and Milner's Discovery
            - Studying learning
            - Had rats running around in mazes
            - Testing stimulating part of the brain
            - Rats kept came back to get more stimulation
            - They discovered the reward system in the brain
            - Mesotelencephalic dopamine system
            - Mesocortico-limbic pathway is most involved with anticipation of reward
            - Nucleus accumbens*
            - Figure 15.7

- Reward system is activated by
    - Drugs (highjack reward system – flood system with too much dopamine)
    - Food when hungry
    - Water when thirsty
    - Love, cuddling, sex
- **Animal models for studying drug addiction**
    - **Drug self-administration**

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        - Cannula inserted into brain structure
        - The rat presses the level to self-inject a drug, either into an area of its brain or into general circulation
    - **Conditioned place preference**
        - A rat repeatedly receives a drug in one of two distinctive compartments, then on the test, the tendency of the rat now drug free, to prefer the drug compartment is assessed

- **Why do some people become addicts and others do not?**
    - Animal models
        - **Self administration increased by:**
            - Food restriction
            - Social stress
            - Environmental stress
            - Certain behavioral traits (novelty seeking – i.e. a rat is more willing to explore)
        - **Self administration is decreased by**
            - Environmental enrichment
            - Good social interaction (vs. isolation)
            - Access to non drug rewards (i.e. a mate)
    - **Incentive –sensitization theory**
        - Habitual drug taking may become a matter of wanting (incentive) rather than liking (hedonic value)
        - In some (addiction prone) individuals, the incentive value of the drug increase with repeated use, even when the actual pleasure decreases
        - i.e. it is the anticipation of taking the drug that keeps them going
        - wanting the drug is more powerful than the liking of the drug
- **Why are some individuals more prone to this sensitization?**
    - Difficult to identify
    - Look at brain
    - The activation in brain shifts when brain is being taken
    - Pleasure and reward part of brain : nucleus accumbus***
    - 1.*Eventually activation shifts to dorsal striatum

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    - a healthy persons brain is different than a drug dependent brain
- 2. In a drug brain some functions are weakened, making inability to inhibit behavior
- Strong influence over limbic areas (emotions)
- **In habitual drug takers**
    - Striatal activation in drug taking shifts from ventral striatum (nucleus accumbens) to dorsal striatum (habit formation)
    - Also impairments in prefrontal cortex and its control over limbic areas (problems with inhibitory control)
- A vicious circle
- Incubation can increase cravings that occur in response to drug cues over time

- **Why some people not others?**
    - Genetic influences (differences in reward value of drugs, inhibitory control)
    - Type II alcoholism is more genetically inherited
    - Biological influences
        - When mothers drink while pregnant: greater disposition for alcoholism
    - Experiences (stress, trauma)
    - Lack of alternative reinforcers
    - Social factors
        - Around others who use drugs and drink
- **Famous Drug Abusers**
    - **Sigmund Freud**
        - Investigated effects of cocaine on fatique, depression and morphine addiction (among other things), often using himself as the test subject
        - Effects of cocaine were not totally understood at that time
        - Published "über coco" (song of praise) in 1884
        - Died from tobacco, got mouth cancer, had many operations
    - **William James**
        - Case of anhedonia

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        - Wrote about the profound mystical revelations he experienced while under the influence of nitrous oxide (laughing gas)

- **Tobacco** (psychoactive ingredient: nicotine)
    - Nicotine (a teratogen) acts on cholinergic receptors in brain
    - Tobacco is leading cause of preventable death (5 million premature deaths/year
    - 70% of people who try smoking become addicted
        - addiction starts within a few weeks
        - 20% of attempts to quit are successful
        - addiction has a major genetic component (heritability estimate is 56%)
    - 10% who try alcohol become addicted
    - 30% who try heroin become addicted
    - Smokers Syndrome: chest pain, labored breathing, wheezing, coughing and more susceptible to respiratory infections
- **Alcohol** (depressant: depresses neural firing)
        - Low doses can stimulate neural firing and facilitate social interaction
        - Major genetic component (heritability estimate = 50%)
        - involved in over 2 million deaths/year
        - 76 million people are heavy users
        - alcohol molecules are small and soluble in fat and water they invade all parts of the body
        - blood levels reach 0.5% = risk of death from respiratory depression
        - alcohol is a diuretic: increases production of urine by the kidneys
        - produces tolerance and physical dependence
        - most alcohol tolerance is functional
        - full blown alcohol withdrawal syndrome
            - 5-6 hours after drinking: severe tremors, agitation, headache, nausea, vomiting, abdominal cramps, sweating and sometimes hallucinations
            - 15-30 hours after: convulsive activity

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        - day or two after: lasts for 3-4 days delirium tremens (DTs): hallucinations, delusions, agitation, confusion, hyperthermia (high body temperature), tachycardia (rapid heartbeat). Can be lethal
    - indirectly causes Korsakoff's syndrome
    - scars liver (cirrhosis) = major cause of death

- **Marijuana** (cannabis sativa flower)
    - Stems used to make rope
    - No resemblance to opiate narcotics
    - **Experience at social dose**: increased sense of well being, restlessness, hilarity, dreamy, carefree state, increased sense of touch, sight, smell, taste, sound. Crave sweets, expansion of space and time
        - Does not appear noticeably different
    - **High doses:** impaired short term memory, slurred speech, meaningful conversation is difficult, paranoia, motor impairment
    - Low addiction potential
    - Produces elevated heart rate (tachycardia)
    - Cannot prove using causes brain damage, or memory problems
    - More likely to be diagnosed with schizophrenia
    - **THC:** suppresses nausea, vomiting in cancer patients
        - Stimulates appetite of AIDS patients
        - Blocks seizures
        - Reduces anxiety, and some symptoms of multiple sclerosis
- **Cocaine and Other Stimulants**
    - Stimulants: increase neural and behavioral activity
    - Cocaine hydrochloride was used a local anesthetic
    - Cocaine's effects: feel self-confident, alert, energetic, outgoing, fidgety, talkative, don't desire food and sleep as much
    - **Cocaine psychosis:** (sleeplessness, tremors, nausea, hyperthermia, psychotic behavior) sometimes mistakenly diagnosed as paranoid schizophrenia
    - **Amphetamine:** similar to cocaine
    - **Empathogens:** psychoactive drugs that produce feelings of empathy
    - Cocaine and its derivatives block dopamine transporters

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- **Opiates: Heroin and Morphine**
  - Opiates bind to receptors whose normal function is to bind to endogenous opioids
  - Effective as analgesics (painkillers)
  - Effective in treating cough and diarrhea
  - Highly addictive
  - Minor health hazards: constipation, pupil constriction, menstrual irregularity, reduced sex drive
  - Heroin rush: wave of intense abdominal, orgasmic pleasure that evolves into a state of serene, drowsy euphoria
  - Methadone is used as treatment for heroin addiction
- **TEXTBOOK TEST:**
- 1. Drugs that affect the NS and behavior are called **psychoactive drugs**
- 2. The most dangerous route of drug administration is **intravenous** injection
- 3. Drug tolerance is of two different types: **metabolic and functional**
- 4. An individual who displays a withdrawal syndrome when intake of a drug is curtailed is said to be **physically dependent** on that drug
- 5. The before and after design is used to study **contingent drug tolerance**
- 6. The fact that drug tolerance is often **situationally specific** suggest that Pavlovian conditioning plays a role in addiction
- 7. **Buerger's disease** provides a compelling illustration of nicotine's addictive power
- 8. Convulsions and hyperthermia are symptoms of withdrawal from **alcohol**
- 9. Anandamide was the first endogenous **cannabinoid** to be identified
- 10. Cocaine sprees can produce cocaine psychosis a syndrome that is similar to **paranoid schizophrenia**
- 11. Morphine and codeine are constituents of **opium.**
- 12. **Heroin** is a semisynthetic opiate that penetrates the blood-brain barrier more effectively than morphine
- 13. **Swiss** heroin addicts were among the first to legally receive heroin injections from a physician for a small fee.
-

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- **Sections 6.5-6.6**
- A system of arbitrary symbols that we agree translates into certain meanings and sounds
- Language localization: location within the hemispheres of the circuits that participate in language related activities
- **Paul Broca**
  - Area in frontal lobe = speech production, expressive language
  - In inferior portion of left prefrontal cortex
  - Hypothesized: Programs of articulation stored in Broca's area
    - speech is produced when these programs activate the adjacent area of the precentral gyrus (which controls the muscles of the face and oral cavity)
    - damage to broca's area: speech production damaged, but doesn't affect language comprehension
- **Carl Wernicke**
  - Area in left temporal lobe, at end of superior temporal gyrus, posterior to primary auditory cortex (in the left planum temporale)
  - "cortical area of language comprehension"
  - Speech comprehension, receptive language
  - Suggested that selective lesions (damage) of Broca's area produce a syndrome of aphasia
    - **Broca's aphasia:** Expressive symptoms: normal comprehension of written and spoken language, speech that retains its meaningfulness – but its slow, labored, disjointed and poorly articulated
      - i.e. A patient who was asked about a dental appointment replied haltingly and indistinctly: "Yes…. Monday…. Dad and Dale….. Wednesday nine o'clock…..10o'clock….. doctors…. And…..teeth
  - Selective lesions of Wernicke's area produce aphasia with receptive deficits
    - **Wernicke's aphasia:** Receptive symptoms: poor comprehension of written and spoken language, meaningless speech, but still has superficial structure, rhythm, intonation of normal speech

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        - i.e. A patient who was asked to describe a picture that showed two boys stealing cookies reported smoothly: "Mother is away here working her work to get her better, but when she's looking the two boys looking the other part. She's working another time"

- Brain Areas
    - **Broca's area** = frontal operculum
    - **Wernicke's area** = planum temporale
        - **Arcuate fasciculus:** pathway connecting these two areas
            - Damage here: is called conduction aphasia
                - No trouble speaking or comprehending, but trouble repeating what people said
    - **Primary auditory cortex**= Heschi's gyrus
    - **Angular gyrus** (left temporal and parietal cortex, posterior to Wernicke's area) Joseph Jules Dejerine**:** written language
        - Discovered during postmortem exam on patient
            - Damage: alexia (inability to read) and apraphia (inability to write)
            - Input from primary visual cortex
        - Left angular gyrus: responsible for comprehending language related visual input (which is received directly from the adjacent left visual cortex and indirectly from the right visual cortex via the corpus callosum)
    - Many scholars (Freud) opposed these ideas
    - 1960's Norman Geschwind revived old localizationist ideas and added new data creating Wernicke-Geschwind model
- **7 Components of Wernicke-Geschwind model** (main theory of language localization) all in left hemisphere
- **1. Primary Motor Cortex**
- **2. Broca's Area**
- **3. Primary Auditory Cortex**
- **4. Wernicke's area**
- **5. Angular Gyrus**
- **6. Primary Visual Cortex**
- **7. Arcuate Fasciculus**
    - **1. Question heard**

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- auditory signals triggered by speech of other person are received by primary auditory cortex and conducted to Wernicke's area where they are comprehended
- if a response is needed, Wernicke's area generates the neural representation of the thought underlying the reply and it is transmitted to Broca's area via the left arucate fasciculus
- in Broca's area the signal activates the appropriate program of articulation that drives the appropriate neurons of your primary motor cortex and your muscles of articulation
- **2. Reading Aloud**
- signal received by primary visual cortex is transmitted to left angular gyrus which translates the visual form of the word into its auditory code and transmits it to Wernicke's area for comprehension
- Wernicke's area triggers the appropriate responses in arcuate fasciculus, Broca's area and motor cortex to elicit appropriate speech sounds

Most important thing to know about W-G Model: IT'S MOSTLY WRONG

- Its partly right, but its too simplistic
- It was based on case studies of aphasic patients with strokes, tumors, penetrating brain injuries
    - Damage is diffuse (widespread), lesion sites connect to other parts of the brain

The Evidence (or lack of)

- Cutting out of Broca's area has no lasting effects on speech (and temporary ones likely due to edema) edema: swelling
    - You can live and speak perfectly fine without it
- Removal of much of Wernicke's area has no lasting effects on language
- Ditto for effects predicted by W-G model by discrete lesions to arcuate fasciculus and angular gyrus
- Large lesions produce aphasia, but usually mixed expressive and receptive problems
    - Expressive: speaking
    - Receptive: understanding

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- Some aphasics don't even have damage to the W-G areas
- Aphasics almost always have damage to subcortical white matter
- **Global aphasia**: (a severe disruption of all language related abilities) is usually related to massive lesions of anterior cortex, posterior cortex, and underlying white matter
- major differences in the locations of cortical language areas in different people

Correct parts in W-G model

- Anterior lesions are more likely to disrupt speech than large posterior lesions
- Large Anterior damage is associated more with expressive deficits
- Large Posterior damage is associated more with receptive deficits
- Important roles are played by Broca's and Wernicke's areas – many aphasics have damage that includes these areas (but is not restricted to these areas)
- Other observations have not confirmed the rest of the predictions of the W-G model
- *model is a very important theory
- *Broca's and Wernicke's aphasias are still used as diagnostic categories, but syndromes are less selective, and damage is more diffuse
- *model is largely abandoned by research because of lack of empirical research, but still used in classrooms and clinics

Electrical Stimulation to Cortex on Language Abilities

(Wilder Penfield 1940)

- purpose was to map language areas so tissue involved in language could be avoided during the surgery
- assessed responses of conscious patient under local anesthetic, stimulation applied to various points on the cortical surface
- electrical stimulation is more localized than lesions
- sites at which stimulation blocked/disrupted speech was scattered throughout frontal, temporal, parietal cortex not just Wernicke-Geschwind areas
- found no tendency for certain kinds of speech disturbances to be made from certain areas of the cortex**,** it was all intermingled
- right hemisphere stimulation almost never disrupted speech

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- **Ojemann's findings related to W-G Model**
  - Areas of cortex at which stimulation could disrupt language extended far beyond the boundaries of the W-G language areas
  - Each of the language tests was disrupted by stimulation at widely scattered sites
  - Major differences among the patients in the organization of language abilities
  - Ojemann believed: language cortex is organized like a mosaic with the discrete columns of tissue that perform a particular function are widely distributed throughout the language areas of the cortex

- TEXTBOOK TEST – Wernicke-Geschwind Model
- 1. The **angular gyrus** translates the visual form of a read word into auditory code
- 2. The **primary motor cortex** controls the muscles of articulation
- 3. The **primary visual cortex** perceives the written word
- 4. **Wernicke's area** is the center for language comprehension
- 5. The **primary auditory cortex** perceives the spoken word
- 6. **Broca's area** contains the programs of articulation
- 7. The **left arcuate fasciculus** carries signals from Wernicke's area to Broca's area

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- 17.1
- Phineas Gage: tamping iron went through head
  - Damage affected both medial prefrontal lobes (planning and emotion)
- **James -Lang Theory of Emotion**
  - Emotions produce certain physiological effects
    - i.e. fear → causes heart to beat faster
  - we notice the effects that are happening, and based on that we feel the emotion
    - oh my heart is beating, I must be afraid
  - emotional experience depends entirely on feedback from autonomic and somatic nervous system activity
- **Canon -Bard Theory**
  - Physiological responses happening, subjective response of emotion happens, but they are separate processes
  - There aren't distinct profiles for emotions
  - Emotional feedback is independent from autonomic/somatic nervous system activity
- Autonomic/somatic feedback not necessary for emotion, but they influence it
- **Modern Biopsychological View**
  - Perception of the emotion-inducing stimulus, autonomic/somatic responses to the stimulus, experience of emotion all influence each other
- **Darwin's Theory of Emotion Evolution** (1872)
  - Expressions of emotion evolved from behaviors that indicate what an animal is likely to do next
  - If the signals provided by such behaviors benefit the animal that displays them, they will evolve in ways that enhance their communicative function, and their original function may be lost
  - They allow you to predict another persons emotion
  - Sometimes its better for you if others what you are going to do next
    - i.e. they run away, avoid a fight
    - thus, emotional expressions evolve
  - gulls: aggression = point beaks at each other

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    - submission = pointing beaks away
- primates: aggression = staring
    - submission = averting gaze

- **Principle of Antithesis**
    - Opposite messages are often signaled by opposite movements
    - Body cues play a major role in human emotion

- **Sham Rage:** exaggerated, poorly directed aggressive responses of decorticate animals (decorticate: cortex removed)
    - Aggressive responses are abnormal for 2 reasons
        - Inappropriately severe
        - Aggression is not directed at particular targets
    - Sham rage can happen in cats whose cerebral hemispheres have been removed to, but not including the hypothalamus
    - Sham rage can't happen if the hypothalamus is removed
    - Hypothalamus is critical for expression of aggressive responses
    - Function of cortex is to inhibit and direct aggressive responses

- **Limbic System and Emotion**
    - **Papez said**: emotional expression is controlled by several interconnected nuclei and tracts that surround the thalamus
        - Emotional states are expressed through the action of the other structures of the circuit on the hypothalamus and they are experienced through their actions on the cortex
        - Paul Maclean expanded theory → "Limbic Theory of Emotion"
    - limbic means border
    - Limbic system includes: amygdala, mammillary body, hippocampus, fornix, cortex of cingulate gyrus, septum, olfactory bulb, hypothalamus

- **Kluver-Bucy Syndrome**
    - Behavior in monkeys whose anterior temporal lobes had been removed
    - Behavior includes: eating almost anything that is edible, increased sexual activity towards inappropriate objects, tendency to repeatedly investigate familiar objects, investigate objects with mouth, lack of fear
    - In primates: symptoms result from damage to amygdala (role in emotion)

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- **Emotions and the Autonomic Nervous System (ANS)**
  - Two important questions
    - **Which patterns of ANS activity are associated with specific emotions?**
      - James-Lange: Different emotional stimuli induce different patterns of ANS activity and these different patterns produce different emotional experiences
      - Cannon-Bard: all emotional stimuli produce same general pattern of sympathetic activation, which prepares organism for action
      - There is not a separate ANS profile for each emotion (contrary to James-Lange theory)
      - Evidence shows: not all emotions are associated with the same pattern of ANS activity
      - No evidence that each emotion is characterized by a different pattern of ANS activity
      - **Are ANS measures effective on polygraph** (lie detector)**?**
      - Polygraphs are still used, but limited
      - Polygraphy: detects emotions, not lies
        - Uses ANS indexes of emotion to infer truthfulness
        - By measuring physiological responses in body
          - Blood pressure cuff
          - Heart monitor
          - Pneumographs
          - Measure pupil dilation
          - Galvanometers
      - **Polygraph techniques**
        - **Control Question Technique**
          - Physiological response to a target question is compared with response to control question i.e. asking neutral questions to counteract nervousness, or questions where the answer is known
          - Success rate in studies is about 80%
          - **Guilty Knowledge Technique**

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        - Ask a question that only the culprit would know the answer to
        - Success rate in distinguishing guilty vs. innocent was 88% in one study
    - **Another way to detect lies**
        - **Microexpression:** brief facial expressions reveal true feelings and may break through false ones
        - Contempt: lip corner tightened and raised only on one side of face
        - Sadness: dropping of upper eyelids, losing focus in eyes, slight pulling down of lip corners
- Paul Eckman
    - Cross cultural research on emotion recognition in New Guinea
    - Different cultures make similar facial expressions
- **Primary Facial Expressions**
    - Surprise, anger, sadness, disgust, fear, happiness
        - All other facial expressions are mixtures of these emotions
- **Facial Feedback Hypothesis:** facial expressions influence emotional experience
    - Test: happy faces made participants feel more happy
        - Angry faces made them feel more angry
- **Duchenne smiles, or all lies**
    - Check the orbicularis oculi (crinkles around eyes)
        - Zygomaticus major (pulls the lip corners up)
- **Facial Expressions: Current Perspectives**
    - Six primary expressions rarely occur in pure form (they have subtle variations)
    - Existence of other primary emotions have not been recognized
    - Body cues, not just facial expressions play a major role in expressions of emotion
        - i.e. pride: a small smile, with head slightly tilted back, hands on hips/raised above head/clenched fits with arms crossed on chest
-

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- **Schizophrenia**
  - Paranoia- being watched, people are after them
  - Hallucinations- mostly auditory (voices)
  - Word salad**,** disorganized speech
  - In their own world – disconnect from reality
  - Heterogeneous group of diseases (schizophrenias)
  - Disordered thought, emotion, behavior
  - DSM-5: the diagnostic and statistical manual of psychological disorders
  - One must exhibit at least 2 of the above symptoms to be diagnosed
  - **Positive symptoms vs. negative symptoms**
  - **Positive symptoms** (symptoms that are not present in normal functioning individuals, but present in patients)
    - **Disorganized thought and speech**
      - Impaired sequential thinking (word salad)
      - Loose associations, tangential thinking
        - Making connections that aren't very relative
      - Concreteness of thought, impaired abstraction
    - **Delusions and hallucinations**
      - Delusions of control, persecution or grandeur
      - Mostly auditory hallucinations (voices; Jesus, Satan, president)
    - **Inappropriate or odd behavior**
      - Inappropriate emotion
      - Disregard for hygiene
      - Difficulty performing everyday tasks
      - Echolalia (repeat back what other people say)
  - **Negative symptoms** (symptoms that are not present in normal functioning individuals)
    - Social withdrawal
    - Flat affect (lack of emotional expression)

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        - Alogia (don't speak a lot, quiet)
        - Avolition (little motivation to do anything)
        - Anhedonia (inhibility to experience pleasure)
        - Catatonia (waxy flexibility: frozen in strange posture, but they don't resist when moved) (repeated meaningless motions)
            - Catalepsy (type of catatonic, sitting very rigid and just starring for a long time)
        - **Negative symptoms are harder to treat than positive**
    - With age, symptoms mellow out

- **Neurochemistry**
    - **The dopamine hypothesis**
        - Excess dopamine (DA) in synapses of frontal cortex
        - **Evidence:** earliest drugs to alleviate Schizophrenia also caused Parkinson's symptoms
            - **Cocaine and amphetamine**
                - Too much dopamine activity in synaptic gap, which blocks the reuptake, and continues to bind
                - Increase dopamine and other monoamine levels, and they can trigger psychotic episodes
        - Blocking DA receptors in the mesolimbic tract treats the symptoms of schizophrenia but blocking DA receptors in the nigrostriatal tract causes motor symptoms
    - **HOWEVER**
        - It was later discovered that not all drugs used to treat Schizophrenia reduce DA levels – some block DA receptors on post-synaptic cell
        - Thus the DA hypothesis was revisited:
            - Schizophrenia caused by high levels of activity at DA receptors

- **Drugs for treating Schizophrenia**
    - Called antipsychotic drugs, antischizophrenia drugs, or neuroleptics)
    - Vary in their strength in binding (affinity) for DA receptors
    - Generally, those with higher affinity are better at treating Schizophrenia
        - **But there are exceptions**

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- Haloperidol and similar drugs (**buytrophenones**)
  - Low affinity, but highly effective
  - They do bind to DA receptors: D2 receptors
  - Other types of neuroleptics (phenothiazine's) bind to D1 and D2 receptors
  - **Revision to DA hypothesis**: Schizophrenia caused by hyperactivity at D2 receptors, specifically

- **But D2 hyperactivity is only part of the story**
  - Newer drugs for Schizophrenia (atypical neuroleptics) actually have a weak affinity for D2 receptors
  - They have a higher affinity for other types of DA receptors and serotonin (5HT) receptors

- **Possible role of serotonin**
  - Psilocybin: found in magic mushrooms.
  - Chemical structure similar to psilocybin, lysergic acid diethylamide (LSD), mescaline, etc.
  - These hallucinogens bind to 5HT receptors and act as serotonin agonists
  - Possibly trick postsynaptic cell into thinking it just got a message from the presynaptic cell

- **Structural abnormalities**
  - Enlarged ventricles and reduced brain volume
  - Widespread neuron loss and structural abnormalities, especially in temporal lobes
  - Sulci are wider
  - 45-50% concordance rate in identical twins
  - structural abnormalities could be a consequence of Schizophrenia, but also could be a consequence of the drugs
  - hippocampal cell disorganization

- **Prenatal and early developmental influences**
  - Increased incidence of schizophrenia:
    - **Malnourishment** (children born during famines)
    - **Stress**= higher prenatal exposure to glucocorticoids=higher DA levels in prefrontal cortex
    - **Birth trauma** (e.g. hypoxia)
    - **Prenatal exposure to viral pathogens** (flu season)

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- **Toxoplasma gondii** (parasite that affects NS)

- **Early Ideas**
  - **Parenting Style**
    - First part of 20th Century:
      - Schizophrenogenic mothering
      - Double-bind theory: there's nothing you can do right
    - **But..**
      - Early 1950's, first drug for schizophrenia
      - Showed it was a biochemical disorder
      - Still, abuse, severe neglect, etc. does have an effect

- **ALSO**
  - Low abuse and overdose risk for neuroleptics
  - Minimal withdrawal symptoms
  - No tolerance to therapeutic effects; tolerance to Parkinson's and sedating effects
  - Significant compliance problems (because of undesirable side-effects, especially typical neuroleptics)
    - Zombie like
    - No motivation

- **Important Findings**
  - 1. Individuals who have not been diagnosed with S, but are at risk, display reduced volumes in several brain areas
  - 2. Extensive brain damage exists when patients first seek medical treatment and have their first brain scans
  - 3. Subsequent brain scans reveal that the brain damage continues to develop
  - 4. Damage to different areas of the brain develops at different rates

- _____

- **Affective (mood) disorders: Depression and Mania**
- **Affective:** any psychiatric disorder characterized by disturbances of mood or emotion
- **Bipolar affective disorder:** depressed patients experiencing periods of mania
- **Unipolar affective disorder:** depressive patients who do not experience mania

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- **Reactive depression:** depression triggered by a negative experience
- **Endogenous depression:** depression with no apparent cause
- **Postpartum depression:** woman gets depression after giving birth
- **Depression: Diagnosis using DSM V**
- For more than two weeks, show at least 5 symptoms
  - Sleep disorder (increased or decreased)
  - Interest deficit
  - Guilt
  - Energy deficit
  - Low mood
  - Inability to maintain social contacts
  - Inability to work
  - Loss of personal hygiene
  - Concentration deficit
  - Appetite disorder
  - Psychomotor retardation or agitation
  - Suicidal
- **Major Depression**
  - Approximately 10-15% of North Americans will suffer from major depression at some point in their lives
  - The majority of cases emerge before 40
  - Can be reactive (someone dies, lose job, traumatic event) or endogenous (endogenous: internal, no outward obvious cause)
  - Depression often recurs: if you've had a depressive episode, you are at higher risk of having another one
  - Rate of depression is about twice as high in women
    - Women are more prone to seeking help, recording it
    - Doctors are more biased in diagnosing women
- **Antidepressant drugs**
  - **First Generation antidepressants**
    - MAO-inhibitors (Iproniazad, Nardil)
    - Tricyclic drugs (imipramine, Elavil)
  - **Second Generation antidepressants**
    - SSRIs (Prozac, Celexa, Paxil, Zoloft)

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- **Third generation antidepressants**
  - Remeron, Effexor
- All act in different ways on monoamines:
  - Serotonin, norepinephrine, Dopamine
- **Comorbidity:** tendency to occur together in same individual

First Generation Antidepressants

- **MAO-inhibitors** (monoamine oxidase inhibitors)
  - Monoamine oxidase: an enzyme that breaks down MAs in the cytoplasm of cells
  - MAO-inhibitors inhibit the action of this enzyme, and the MA levels rise
  - **Problem:** MAO needed in the liver to break down a chemical in many foods (tyramine) that causes very high blood pressure (higher risk of stroke)
  - Patients need to carefully control their diet (wine, cheese)
  - "Cheese effect"
- **Tricyclic antidepressants**
  - Prevent reuptake of MAOs into the presynaptic cell, so more MAs available in synapse
  - No dietary restrictions (do not inhibit MAO)
  - **Problem:** high doses can lead to irregular or quickened heartbeat (not suitable for patients with cardiovascular disease)

***Drugs are often discovered accidentally** (e.g. Viagra)

Second Generation Antidepressants: SSRISs

- **Selective Serotonin Reuptake Inhibitors**
  - Raise functioning levels of serotonin, specifically, by slowing down its reuptake into the presynaptic cell
  - Safer for cardiovascular patients, and relatively few side effects
  - **Problems:** agitation, nausea, sexual dysfunction, increased risk of seizures

Third Generation Antidepressants: SNRIs

- **Selective-norepinephrine reuptake inhibitors**

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- **(serotonin-norepinephrine reuptake inhibitors)**
    - raise functioning levels of norepinephrine (NE) and sometimes also serotonin by inhibiting their reuptake
    - SNRIs avoid the adverse effects of the tricyclic's on the cardiovascular system

Monoamine theory of depression

- Depression caused by under activity at serotonergic and noradrenergic synapses
- Support
    - Drugs that increase activity at these synapses help
    - More 5HT and NE receptors in brains of depressed people (unregulated to make best use of NTs)
- But its not that simple

Neuroplasticity Theory

- Depression caused by decrease in neuroplastic processes in prefrontal cortex, hippocampus, amygdala
- Support:
    - Stress and depression reduce neurotrophins and neurogenesis
    - Antidepressant treatments increase neurotrophins and neurogenesis
    - Ketamine increases synaptogenesis, and alleviates depression in a day (but it has high abuse potential, so it isn't prescribed)

*Depressed brains have a suppression of activity compared to healthy brains. Hyperactivity in amygdala (structure involved in fear, anxiety)

Sympatholytics

Beta Blockers:

- Beta adrenergic receptor antagonists
- Block catecholamine receptors in the sympathetic nervous system (especially the heart muscle)
- **Applications to PTSD**

Anxiety Disorders

- **Generalized anxiety disorder** (high level of anxiety majority of the time for no particular reason)

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- **Panic disorder**- extreme sympathetic arousal, no particular cause
- **OCD**: obsessive compulsive disorder, anxiety of behavior and thoughts
- **Phobic Anxiety Disorder**: phobia is cause for panic attack
- **PTSD**: caused by trauma. Experience trauma multiple times later in life, continue to suffer effects
- **Main brain areas involved**:
    - Hypothalamus
    - Amygdala (emotions, fear, anxiety)
- Decreased activity in inhibitory NTs (GABA)
- Increased activity of excitatory NTs (Glutamate)

 Anxiolytics (anti-anxiety drugs)

- **Benzodiazepines** most common
    - i.e. Diazep**am** (Valium), Alprazol**am**, (Xanax, Lorazep**am** (Ativan)
- **GABA agonists**: bind to the GABA A receptor complex and facilitate effects of GABA
- ***Alcohol binds to same sites as GABA = don't mix!!!

 Sympatholytics

- **Beta Blockers:** beta adrenergic receptor antagonists
    - Adrenergic receptors bind the catecholamine NTs norepinephrine and epinephrine
    - Receptors found in cells of heart, lungs, arteries, stomach and other organs in the sympathetic nervous system
    - Binding of catecholamine's to beta receptors stimulates sympathetic response
    - Beta blockers block the physiological effects

 Overcoming fear, once and for all

 Propranolol (beta blocker): heart problems, migraines, tremors, stage fright

- A possible treatment for PTSD
    - NE (norepinephrine, or adrenalin) associated with memory consolidation
    - If propranolol given immediately after trauma, memory consolidation disrupted

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- May even be useful in weakening memories years after trauma
  - When the event is remembered, the memory trace becomes labile
  - It can then be either reconsolidated or extinguished
  - Administering propranolol interferes with reconsolidation
  - NOTE: still in early experimental stages – efficacy unknown

- **Tourette Syndrome** (disorder of tics)
  - **Tics:** involuntary, repetitive, stereotyped movements/vocalization
  - Typically begins early in life with simple motor tics
    - i.e. eye blinking, head movements
  - symptoms become more complex and severe with age
    - i.e. hitting, touching objects, squatting, hopping, twirling, dirty gestures
    - common verbal tics: barking, coughing, grunting, coprolalia (uttering obscenities), echolalia (repetition of another's words), palilalia (repetition of owns own words)
    - 3 times more common in males
  - some also display signs of ADD, OCD or both
  - tics can be suppressed if patient puts in enough effort
  - use brain imaging to study syndrome
  - patients have smaller caudate nuclei, thinning in sensorimotor cortex
  - decision to suppress tics comes from prefrontal cortex
  - hypothesis: disorder is related to abnormality of the basal ganglia-thalamus-cortex feedback circuit
  - **Treatment**
    - Treatment focuses on aspects of disorder other than tics first
    - 1. Educates family and friends about syndrome
    - 2. Focuses on emotional problems (i.e. anxiety, depression)
    - 3. Tics are treated with neuroleptics (can reduce by 70%)
      - often refused because of side affects
        - weight gain, fatigue, dry mouth

- **Clinical Trials: Development of New Psychotherapeutic Drugs**

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- **Translational research:** research designed to translate basic scientific discoveries into effective clinical treatment
    - **Clinical Trial Phases**
        - **1.** Screening for safety (finding maximum safe dose)
        - **2.** Establishing test protocol
            - dose drug is therapeutic at, how frequently it needs to be administered, and how long does the drug need to be taken
            - placebo control groups used, double blind study
        - **3.** Final testing
            - usually 2 successful tests needed (beneficial effects are greater than adverse side effects)
        - government reviews process before and after human trials
- **Active placebos:** control drugs that have no therapeutic effect, but produce similar side effects to drug being studied (so placebo group doesn't realize that they are receiving placebos)
    - Only 22% of drugs that enter phase 1 make it
    - Sponsoring drug company often makes scientists agree not to publish/discuss negative findings without company's consent
        - Any new drug looks promising if negative evidence is censored
    - Drug companies rarely fund research for drugs for rare disorders because it's too expensive and not profitable
    - **Orphan drugs:** drugs that are too small for the market to be profitable
    - **Translational bottleneck:** only a small portion of ideas/treatments receive funding

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